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TRENCH FEVER

W. BYAM

OXFORD MEDICAL PUBLICATIONS

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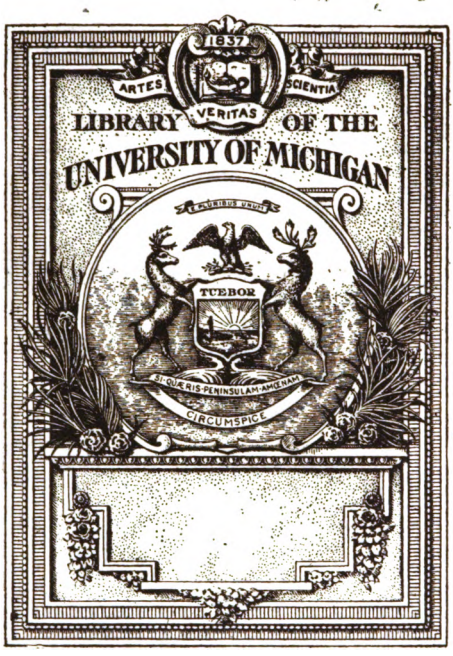

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TRENCH FEVER

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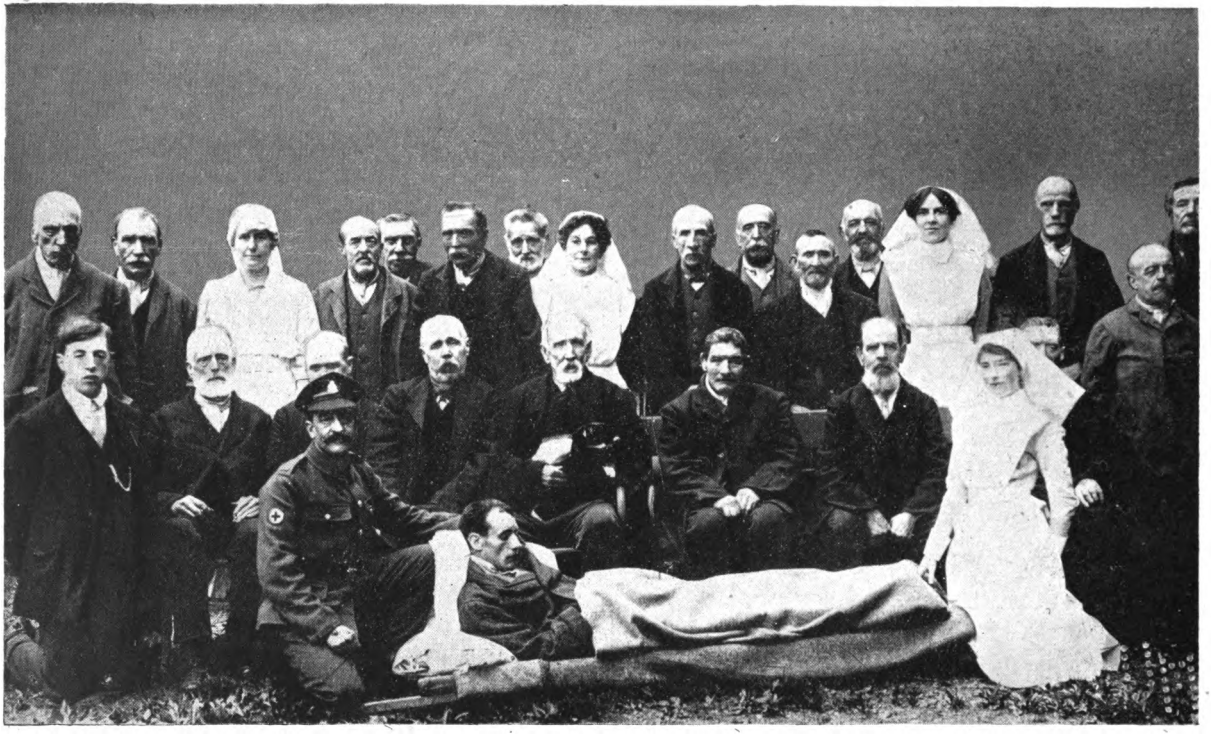

Some of the men who volunteered for the experimental work and nursing staff.

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TRENCH FEVER

A LOUSE-BORNE DISEASE

BY

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A FOREWORD BY
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AND A SUMMARY OF THE REPORT OF THE AMERICAN
TRENCH FEVER COMMISSION BY
LIEUT. R. H. VERCOE, R.A.M.C.

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PREFACE

THE work on which this account of trench fever is based has been carried out at Hampstead for the War Office Trench Fever Investigation Committee, of which Major-General Sir David Bruce, K.C.B., F.R.S., A.M.S., is Chairman. The members are :

Lieut.-Col. D. Harvey, C.M.G., R.A.M.C. ;
A. W. Bacot, Esq. ;
Major W. Byam, R.A.M.C. ;
Lieut.-Col. H. French, R.A.M.C. (Temp.) ;
J. A. Arkwright, Esq. ;
Sir W. M. Fletcher, K.B.E., F.R.S. ;
Lieut. A. F. Hird, Gen. List (Temp.), Secretary ; and until recently
The late Professor H. Plimmer, F.R.S.

It may be mentioned here that the expenses connected with the experimental work of the investigation were defrayed by the Lister Institute.

Trench fever has come into prominence during the present war, and has been responsible for a greater amount of sickness than any other infection on the Western Front. It would be a mistake, however, to regard it as a disease of war only. It is more than probable that the fever was well recognised in ancient times, and Werner (*Berliner Klin. Woch.*, Feb. 1917) mentions that he came across an epic poem of the twelfth century, called *Meister Isengrimmus*, in which the following hexameter appeared : 'aut habet aut fingit quintanae frigore febris '—'he has or simulates the rigor of five-day fever.' Werner adds : 'That seemed to me very remarkable, so that I took the trouble to look through the ancient literature, and found quite a number

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of other statements to prove that this fever—characterised by recurring attacks at five-day intervals—was known in ancient, mediæval, and also in later times. There are passages in Galen and Hippocrates alluding to five and six day fevers, as also in the Arabic writings, and an author known as Gilbert of England describes a similar fever recurring every five and six days. The literature of malaria shows a few references to five and six day fevers which were considered akin to that disease till the parasite of malaria was discovered and a certain differential diagnosis made possible.'

Probably trench fever has existed from ancient times, and there is reason to suppose that it may become a disease of peace once more unless its character, mode of spread, and intermediate host—both the body louse and the head louse —are understood by the profession at large.

From what we have seen of experimental trench fever infections, it is probable that most of the mild and indefinite attacks of pyrexia of uncertain origin occurring in the army must be attributed to the same source as recognised cases of this disease. The total number of those who have suffered during the war then becomes appalling, and of this vast total very many, not only of the slight unrecognised cases but also of diagnosed cases which are deemed to have recovered, will still remain infective on their return to civil life. Steps must be taken to prevent the spread of their infection, for those affected are in many instances permanently unable to resume their former occupations, and many have already passed back from the army to civil life incapacitated and a charge upon the State. Should this process continue in civil life the drain upon the labour resources of the nation will be most disastrous at a time when man-power is of the highest value. It is not too much to say that there is every reason to suppose that, unless adequate measures are taken to prevent it, the disease may

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arise and spread wherever lice are prevalent, provided that men already infected are sent there from endemic areas. Considering the world-wide distribution of the louse, this is a very serious matter.

To emphasise further the importance of trench fever, we would state at once that, in its later stages, it is the direct cause of a large percentage of the cases of disordered action of the heart, or the 'irritable heart of soldiers,' of neurasthenia, neuralgia, and rheumatism now filling the beds of our hospitals and at our spas. Carmalt Jones (*Lancet*, October 5, 1918) has recently produced evidence showing that trench fever is a very serious source of invaliding, and makes the statement that 'among 100 cases of D.A.H. taken at random and serious enough to reach a heart centre, two out of three were due to trench fever alone, and eight out of nine were due to this infection, at least in part.'

Any campaign undertaken to combat the disease must be supported by even more vigorous measures against scabies than those taken at present, for the etiology of trench fever is intimately connected with the incidence of that disease. The sufferer from scabies presents skin lesions which predispose to infection with trench fever and scratches himself in a way that will ensure inoculation if the trench fever virus is present.

While still looking to the destruction of lice as our best hope for controlling the disease, all efforts should now be turned to the production of a treatment which will render the blood of a trench fever patient incapable of infecting lice. Our present methods of treatment do nothing to this end, and must therefore be improved. Not only is this necessary in the interests of those in the field and at home, but in order to prevent men already infected from becoming the unhappy invalids whose condition at present time alone

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can cure. The organism of trench fever should be our chief quest, as knowledge of its nature is essential to sound work on the production of a specific therapy.

In the following pages an account is given of the work already accomplished in this important direction.

We would like to add that our researches have been supported by the loyal and unselfish help of two ladies, Miss Eve Dickson and Miss Sheena Tennant, to whom we offer our sincere thanks.

W. B.

HAMPSTEAD.

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INTRODUCTION BY LIEUT.-GENERAL SIR T. H. GOODWIN, K.C.B.

I HAVE watched Major Byam's work on this subject with very keen interest, and have had the privilege of attending his lecture.

I am very glad to think that his important investigations are being published, and feel that they will be of very great value.

T. H. GOODWIN, *Lt.-General*,
D.-G.

11.6.18.

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FOREWORD BY MAJOR-GENERAL SIR DAVID BRUCE, K.C.B., F.R.S., A.M.S., Chairman, War Office Trench Fever Committee.

MAJOR BYAM and his co-workers are to be congratulated on the progress they have made in the study of this most interesting disease, trench fever. Typhus fever seems to be a near relation, but differs among other things in the rate of mortality; trench fever is never fatal, or at least no fatal case has up to the present been recorded.

Another curious and interesting thing about trench fever is that it seems to have appeared on the Western Front wholly unexpectedly, like a bolt from the blue. Nothing seems to have been known of it before the war. All the early writers in France suggested that the disease only arose in the trenches or among orderlies who came into close contact with the sick. The late Professor Plimmer held the theory that the disease was the same as that called 'Sweating Sickness,' which broke out in our armies in France in the early wars in the time of Henry VII. But it is difficult to identify a protean disease such as this from mediæval description.

In regard to the carrier of this disease, we must really felicitate the louse on at last emerging from its seclusion and crawling into the full light of notoriety. The high positions hitherto held by the mosquito, the tsetse, and the flea are apparently about to be usurped by the louse. From being an object of fear and contempt, the mere mention of whose name was looked upon as a deadly sin, the louse is now an object of interested curiosity in the best society.

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As to when the louse was first suspected of being the carrier of this disease, it is difficult to give the exact date. Trench fever was probably present among our troops in the winter of 1914-15, but not at first suspected to be a new form of disease. In April 1915 suspicion was aroused, and in September, Graham, and, in November of the same year, Rankin and Hunt described its clinical features.

In July 1916 Herringham rather tended to oppose the louse theory, but in the same month we find Hunt and McNee writing that they think sufficient proof has now been obtained that the body louse is the parasite concerned, although absolute proof is lacking, as they had been unable to carry out actual transmission experiments.

Even as late as March 1918 we find Sundell and Nankivell stating that, considering the evidence for and against the propagation of trench fever by means of lice, they can only say that transmission by lice is not proven.

Certain investigators have experimented on themselves by allowing infected lice to feed upon them. Jungmann let a louse bite him, and showed symptoms after twenty-seven days ; Davies and Weldon took two pairs of lice and fed them for fifteen minutes on a trench fever patient, and then immediately on themselves. One pair was further fed on one of them next day. Twelve days later the latter developed trench fever.

Werner and Benzler fed five lice upon an acute case, and for the following eight days on Werner. Eight weeks later Werner developed the fever, but he had six months previously suffered from the disease.

It is quite evident, from our present knowledge of infection and incubation, that all these experiments were useless for the purpose, and may be washed out. To the War Office Trench Fever Committee, then, is due the honour of having been the first to demonstrate by experiment the

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part played by the louse in the transmission of trench fever. The first experiments on the transmission of the disease by the bites alone were started on the 29th December 1917, and were negative. The experiments with excreta were begun on the 5th February 1918, and the first successful result was obtained on the 14th February. As the question of the priority of a discovery depends on the date of its publication, I may say that this was published on the 23rd March 1918 as an interim report in the *British Medical Journal.*

The American Research Committee in France, however, ran the War Office Committee very closely, and they deserve the very highest praise and admiration for the energetic and businesslike manner in which they took up this research among many others, almost as soon as they arrived in France. The investigation of trench fever was started by them about the end of January 1918. The Americans had great advantages. They had practically any worker, British or American, they asked for, and they at once applied to the Commander-in-Chief to supply sixty volunteers.

In all investigation work of this kind, unless you have at hand an animal susceptible to the disease, you might as well put up the shutters and close down the whole business. In trench fever there is no known susceptible animal except man, and therefore without human volunteers no progress could have been made. This Trench Fever Committee therefore, as well as the Anglo-American, owes everything to the plucky men who volunteered.

On the 14th February 1918 the Anglo-American Committee stated that experiments on louse transmission were still in progress, but no positive results had been obtained.

On the 9th March they reported that, in twenty-one experiments in which louse transmission was attempted,

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four so far had proved positive. The Committee then passed a resolution that, after an examination of these cases, they felt that they had sufficient evidence to say that it had been shown that trench fever is transmitted by the louse.

One of the most important and interesting points in the research remains to be discovered, that is the parasite. Many attempts have been made to find it. Spirochætes and other micro-organisms have been blamed. Several writers have also stated that they consider the parasite to belong to that almost mythical genus the Rickettsia, also described as occurring in the louse in typhus fever. This matter is being investigated, but up to the present nothing very definite has emerged.

D. B.

May 17, 1918.

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CHAPTER I

THE ACUTE DISEASE

Definition of Trench Fever.—As no pathognomonic sign or symptom of trench fever is at present recognised, we would define the disease as a blood infection communicable from man to man by means of the louse (*P. humanus*) and possibly other parasites. It is characterised in its early febrile stage by recurrent pyrexia, headache, giddiness, which early in the disease is generally a true vertigo, pain in the back, pain in the limbs, which is chiefly in the legs and often of very considerable severity, a slow pulse in comparison to the degree of fever, conjunctival congestion, sweating, polyuria, a moderate leucocytosis at the height of the fever, with evidence of blood infection in involvement of the spleen and, in a proportion of the cases, of the liver also.

In some cases a period of unstable temperatures follows. Eventually a certain percentage of the patients pass into a stage of chronic ill-health. These patients suffer from recurrent pains in the limbs, headaches, and nervous manifestations such as mental depression, excessive tendency to sweating, disordered action of the heart (D.A.H.) and abnormal response to stimuli, all of which are accompanied by a mild degree of anæmia and some loss of weight. Damp weather tends to produce exacerbations of all pain in sufferers from the late stages of the disease. The infection, in some cases, is very persistent, and acute febrile relapses may occur after months of quiescence.

The Seasonal Incidence.—We are unable to speak of this

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with certainty, but it appears that the number of infections gradually increases during the cold weather, when a man's own efforts to free himself from lice are accompanied by increased discomfort and when men huddle together in order to keep warm. The number of cases decreases but slowly throughout the warmer months. The incidence must vary directly with the degree of louse infestation in any community.

The following is a **summary of the histories** obtained from 200 consecutive cases of trench fever sent to Hampstead. The **onset** was uncertain in 16 per cent. of these; of the remainder, we have classed 32 per cent. as gradual in onset and 52 per cent. as sudden. Some have been quite dramatic in their suddenness; others apparently only felt giddy or shaky during an hour or two before the attack was ushered in by a 'splitting headache' and weakness so marked that the victim 'could hardly crawl.'

A picture of the sudden onset is as follows: 'Felt perfectly fit; did a heavy day's work without any distress. Suddenly felt giddy and weak and shaky on the legs; splitting headache, shivers and hot sensations alternately; could not get comfortable in bed, ached more or less all over —worse in loins and legs. Got up two or three times to pass water. Slept badly. A little better in the morning, got up, could hardly stand, pains returned severely.' The typical shin-bone pains may come on at once, but as a rule appear considerably later.

Prodromal symptoms in the cases of gradual onset were noted in the following order of frequency: Pain in the head, pain all over, weakness, pain in the legs, malaise, dyspnœa, giddiness, pain in the loins, shivering, pain in the abdomen, diarrhœa, constipation, anorexia, nausea, frequent micturition, restlessness, or insomnia.

The prodromal period lasted for two days or longer. Such prodromata are really the early symptoms of definite onset, as in many cases the severity of symptoms increases

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gradually during the first few days of the disease. It should be noted that the symptoms in a relapse are often more severe than in the initial attack.

Without doubt trench fever is more often sudden in onset than gradual.

Men from all branches of the service become affected with trench fever, nor does any particular previous illness seem to predispose to the condition.

In our series of cases the symptoms of onset occur in the following order of frequency : Pain in the head occurred in 74 per cent., in the shins in 46 per cent., in the loins in 31 per cent., in the knees in 21·5 per cent., in the ankles in 19 per cent., in the thighs in 15 per cent., in the calves in 13 per cent. ; shivering and chilliness in 26 per cent. ; sweating in 19 per cent. ; frequent micturition in 13 per cent. ; dizziness in 12 per cent. ; nausea and vomiting in 11 per cent. ; pain in the shoulders and arms in 8 per cent. ; pain in the abdomen in 7·5 per cent. ; diarrhœa in 5·5 per cent. A similar table including symptoms from the onset to a later period in the disease shows an increase in the frequency of their occurrence, *e.g.* pain in the head 92 per cent., pain in the abdomen 24 per cent., pain in the shins 77 per cent.

Tenderness of the shins, as apart from pain, was remembered by 9 per cent. of the patients as an early symptom, while several referred vaguely to 'feeling sore' and as if 'they had been kicked' on the day of onset. In addition to fever, headache may be the only symptom at the onset of the disease.

There is reason to think that dizziness is much more common than the figure given would indicate. The 'restlessness' complained of bears some resemblance to the discomfort of the 'growing pains' of youth, in that no position of comfort can be found, and so is unlike the pain of rheumatism, where one finds a position of minimum discomfort and is glad to maintain it.

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The **headache** is most commonly felt across the forehead and behind the eyes; but it may be bitemporal, or occipital, or less commonly vertical. Some describe the pain as being right inside the head. Usually one of the earliest symptoms, it is often one of the most severe, persistent and commonly recurrent. It is very rarely associated with tenderness of the scalp. When occipital it is often accompanied by stiffness in the back of the neck. There is often some mental confusion and a tendency to talk excitedly. The character of the **pain in the limbs** is twofold: (*a*) dull aching or gnawing, more or less continuous, always worse at night, and (*b*) acute pain—shooting or stabbing—which may last many hours, especially at night. This latter pain is nearly always felt in the bone, and most frequently in the tibiæ. [Spinal puncture and withdrawal of a small quantity of cerebro-spinal fluid has given speedy relief in some of our cases with very acute leg pains. Sometimes the pains recur, but never so severely. The fluid withdrawn has always been clear, though sometimes under slight pressure].

There is no part of the body which invariably escapes from pain. After a few days, however, the 'pain all over' subsides, and localised pain becomes prominent. The loins and lower limbs are most often affected. Pain is usually but not invariably symmetrical. The situation of the pain may vary from day to day. Certain observers have suggested that there are two distinct diseases at present termed trench fever, and would differentiate them by the presence or absence of shin-bone pain. We are convinced that this is not so, both from clinical observation and experimental work.

When pain is complained of in the joints we have not noticed any concomitant swelling; the joints are sometimes painful or stiff to move, but this is due to pain on movement in the neighbouring structures.

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It will be seen that 7·5 per cent. of the cases had pain in the abdomen within the first twenty-four hours; 24 per cent. complained of it at some time within the first week or two of their illness. In six cases the pain was associated with early diarrhœa.

Of the 24 per cent.,

3 cases complained of pain in the right hypochondrium,
19 ,, ,, ,, left hypochondrium,
13 ,, ,, ,, right iliac region,
13 ,, ,, ,, left iliac region.

The pain in the right iliac region may be so severe as to give rise to a diagnosis of appendicitis.

A case of interest in this connection is reported by Graftenberg (*Deutsche med. Wochenschr.*, Berl. u. Leipz., 1918, 44). 'A soldier, aged twenty-two, was suddenly seized with acute pain and tenderness in the right iliac fossa, fever (103°) and rapid pulse (144). The appendix, which was normal except for the presence of a stercolith, was removed and the temperature fell to normal. Five days later the pain in the iliac fossa recurred, and for twenty-four hours there was fever (101-4°); two more, though slighter, relapses followed at intervals of five and six days before the patient passed from observation.'

The Spleen.—The pain complained of in the left hypochondrium points in most instances to involvement of the spleen. In early cases the splenic region is frequently so tender that examination by palpation is impossible on account of stiffness of the muscles over the organ. An appreciable percentage of all our cases have had palpable spleens during some period of the disease, though such enlargement has never been of more than two fingers' breadths below the costal margin. Such definite enlargement is most often the result of a prolonged infection. The actual size of the spleen, however, varies from day to day in the early stages

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and does not remain constant until late in the disease. (The spleen was palpable early in the disease in the cases whose charts are shown as Nos. 2, 7, 13.)

Pain in the right hypochondrium over the liver points probably to changes in that organ, but how far trench fever is responsible is not clear.

A diagnosis of pleurisy had been made in some of the cases sent to us on account of splenic or liver pain.

A peculiar and very constant feature is the rapidity with which there are **alternations of shivering and sweating,** such alternations occurring several times in the course of a single day or night. True rigors are rare, but have been observed by us, and were very marked in the case whose chart is shown as an instance of four-day fever (Chart 8).

Frequent micturition was complained of by 13 per cent. of our cases, was not associated with pain, but resulted in the passage of an increased amount of urine. The polyuria occurs as the temperature falls, and in two of our cases in which the amount was estimated 110 ozs. and 86 ozs. were passed in twenty-four hours towards the end of the initial attack.

During the acute attack the **pulse rate** is slow in comparison to the degree of fever, and a fairly typical curve is shown in the chart below. It will be seen that the rate rose with each rise of temperature, and that a mild degree of D.A.H. developed in the third week. Such a case may be considered as severe.

A fairly constant feature of the initial attack is a mild degree of **conjunctival congestion**, sufficient to be designated as ' pink eye.' The condition is usually transient, though it frequently recurs with subsequent rises of temperature.

At first the **tongue** is lightly coated with fur, though there is nothing characteristic about its appearance ; it soon clears and often remains remarkably clean.

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Affections of the respiratory tract are usually conspicuous by their absence.

Areas of tenderness are frequently associated with the pains, and may involve the skin, muscles, tendons, bones or joint cartilages. The nerve trunks themselves do not

CHART I

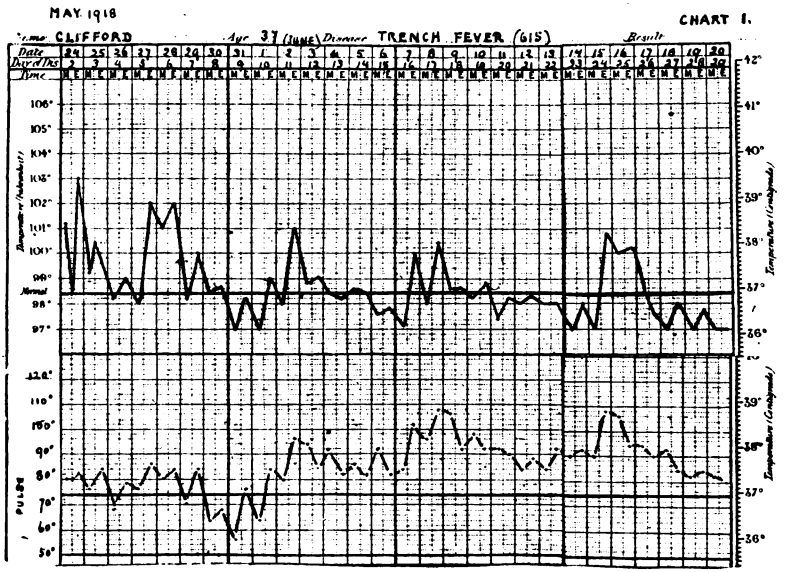

CHART 1.—Relation of pulse rate to temperature curve.

appear to be involved. Such tenderness, in some cases extraordinarily acute, may occur independently of pain, or pain independently of tenderness, and either or both may persist for long periods after the fever has subsided. The extent of the areas of tenderness usually increases with exacerbations of the disease. Such exacerbations may be entirely afebrile ; as with the pain, the areas of tenderness are usually bilaterally symmetrical, with the exception of those over the front of the chest, where it is common to find the skin over the left lower ribs only involved. The

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area of skin most frequently found to be hyperalgesic runs from knee to ankle along the outer border of the tibia.

It would appear that the areas of skin tenderness correspond to the 8th cervical, 1st and 7th dorsal, and the 1st, 2nd, 3rd, 4th, and 5th lumbar segments of the cord. The whole of these segmental areas are involved in comparatively few cases ; those most commonly involved being the lower segments of the lumbar group. These areas were described by us in the *Journal of the Royal Army Medical Corps*, November 1917, and their distribution has recently been carefully defined by Carmalt Jones (*The Lancet*, Oct. 5, 1918). Areas of analgesia may be detected in some of the more prolonged infections, and Sundell (*The Lancet*, Oct. 19, 1918) makes the following observation, with which we agree :— 'This loss of sensibility varies in degree from a mere blunting of sensation to complete analgesia. The most common situations for this phenomenon are the outer surface of the calf, the infrapatellar, scapular, and deltoid regions . . .' and adds that these areas of analgesia . . . 'may still be present in a proportion of chronic cases readmitted to hospital from convalescent camps.'

As curiosities we have observed instances of aphonia during pyrexia, herpes on lips and trunk, dermatographia, flushing of the skin over the tibiæ, and tingling of the fingers and toes.

During an acute attack the patient's general condition obviously deteriorates, and he presents an appearance of exhaustion, the result of constant severe pain and repeated sleepless nights. He steadily loses weight and becomes **anæmic**, though the colour index is rarely below 0·8.

Chart 4 is that of a patient who while with us lost 36 lbs. in weight during five months.

After a period varying from a few days to about a fortnight from the onset of the disease, the acuteness of the patient's pain subsides, he sleeps well, and his appetite

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returns. There is even then generally some return of pain each night in some part of his limbs—most commonly the shins, calves, or ankles. If he is allowed to get up, he finds that walking increases the pain.

During the next week or two, whether pyrexia recurs or not, there are recurrences of symptoms—especially leg-pain, each exacerbation being a short replica of his original attack or of some portion of it. When accompanied by marked pyrexia such recurrences nearly always involve recurrences of headache, pink eye, sweating, and often of polyuria. The muscle or bone pain may at such times occur in hitherto unattacked parts.

In some cases such recurrences are few and slight, and the patient soon feels fit and complains of nothing but slight pain or still slighter tenderness in a limited area of the legs from the knees downwards.

In others the recurrence, even if quite late in the disease as after months of quiescence, may be more severe than the original attack.

PYREXIA

Much confusion seems to exist as to the various temperature curves met with in trench fever, and their relation to one another. Some observers would only accept periodic fevers with shin pains as evidence of this disease. Neither periodic fever nor shin pain is essential.

Although we have carefully considered the various types of temperature charts, we find no constant correlation between the fever curve and the clinical course. Any grouping of symptoms may be found associated with each of the various types. Our experimental work supports this view.

In addition, our experimental infections have provided charts which vary so much in character that it is most difficult to classify them. It is evident therefore that too much reliance should not be placed on the type of temperature curve when making a diagnosis of trench fever.

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Our experimental work has also shown that some cases may be afebrile throughout. A study of the charts in Chapters II. and III. will show that in these undoubted instances of trench fever the temperature curve is often so irregular as to make it possible in the future for us to accept the majority of cases of 'pyrexia of uncertain origin' in the armies as attacks of this louse-borne disease.

It is on the whole true, however, to say that the higher the temperature rises the more likely is the curve to be of an intermittent periodic character, or, in other words, the prolonged, almost daily, fevers are usually low fevers with a maximum but rarely exceeding 101°. It would seem, therefore, that the man with the greater resistance to the infection reacts with a higher degree of fever than the man with less, —that the higher fever is followed by a period of more absolute freedom from fever, and in this way is produced the more definitely relapsing periodic type of chart. This last type of chart we associate (*a*) with relapses, when an outpouring of poison is followed by a prompt febrile response and rapid return to normal, the result of a partial immunity; (*b*) with reinfections, when the same partial immunity has the same effect, though the source of poison is from without instead of from within (see charts in chapter on 'Immunity'); and finally (*c*) with such a small dose on original infection that reaction is quickly complete and return to normal rapid.

In each case such a 'spike' of temperature may be but one of a series, the others not having been observed.

The charts met with may now be considered in order of their simplicity.

Type A.—A fever wave lasting roughly three days—maximum temperature observed by us 104·4°—followed by recovery without relapse. (Charts 2 and 12.) Such cases are usually diagnosed influenza.

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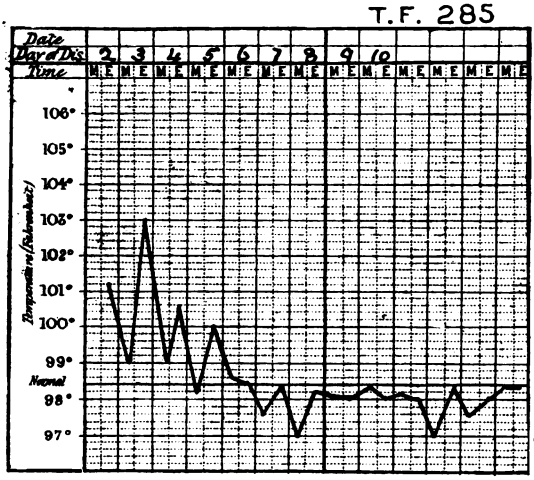
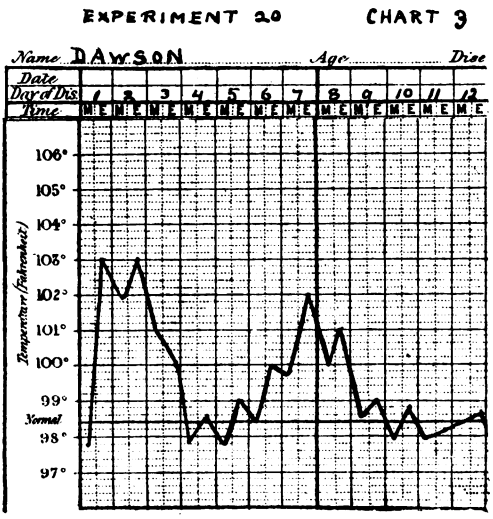
Chart 2—(Type A)



Type B.—A similar wave followed, most commonly on the 6th, 7th, and 8th days, by a febrile relapse, the interval between the initial wave and relapse being afebrile. (Charts 3 and 16.)

Chart 3—(Type B)



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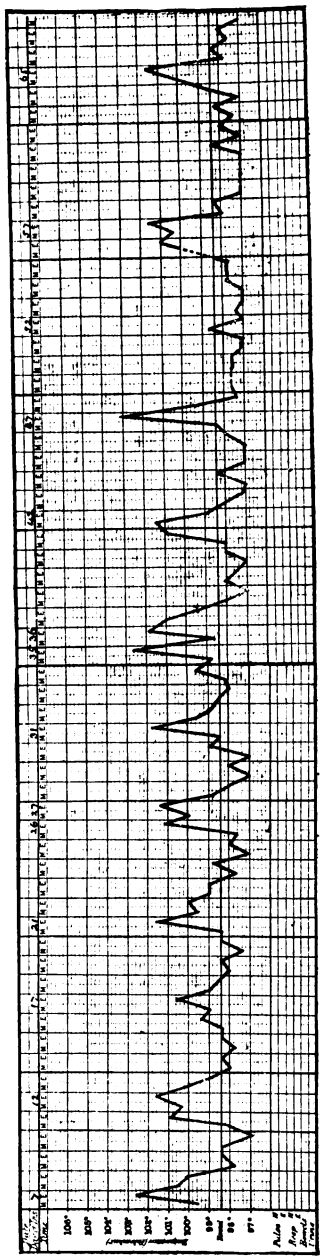

CHART 4—(Type C)

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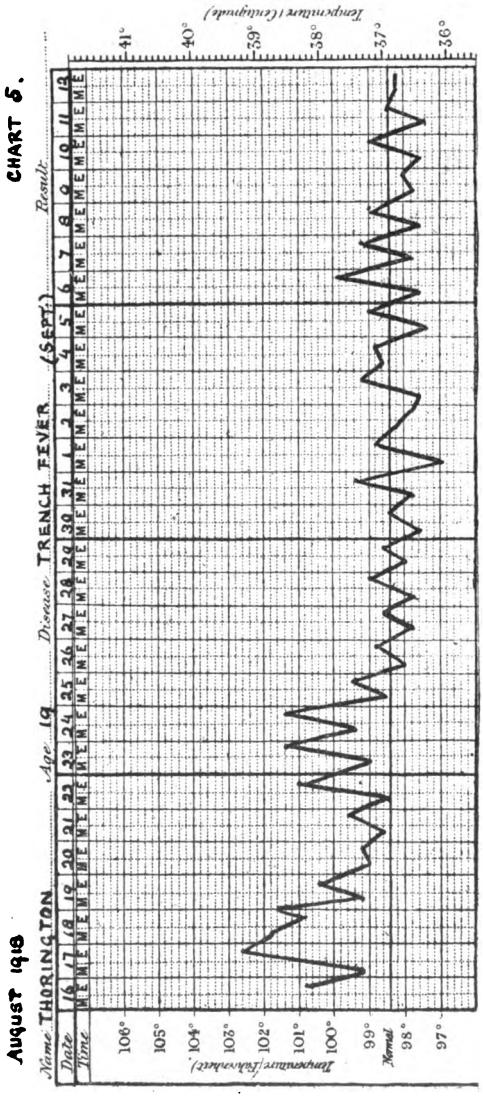
Type C.—The same as B, but followed by further definite relapses with afebrile intervals which are frequently so regular as to give an appearance of periodicity. (Charts 4 and 29.)

Type D.—The same as B, but followed by irregular, almost daily, fever. (Chart 5.)

CHART 5—(Type D)



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Type E.—A continuance, more or less complete, of the original fever wave into the relapse (Charts 6 and 7). Such charts often suggest 'modified typhoid.' They are frequently followed by a prolonged period of irregular fever.

Chart 6—(Type E)

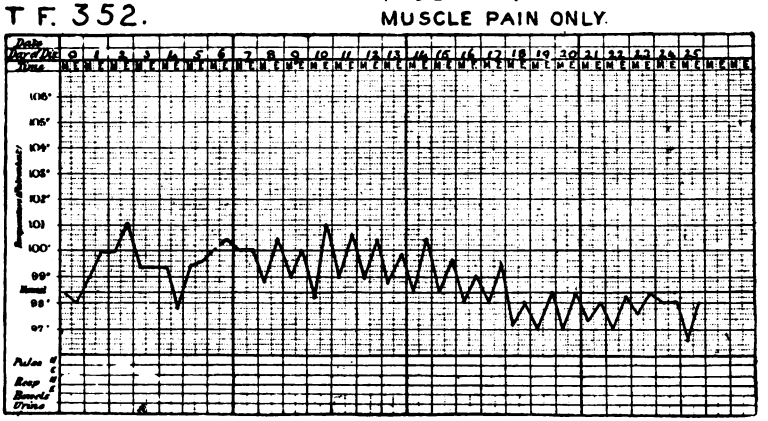
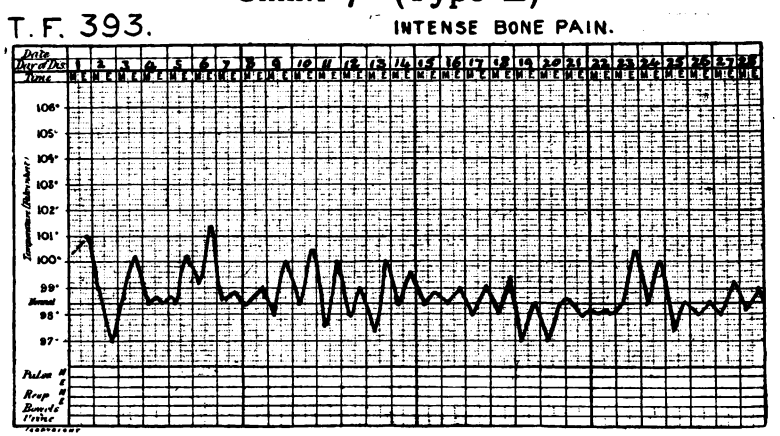


Chart 7—(Type E)



Type F.—Waves of fever of short duration, a few hours only as a rule, separated by afebrile intervals. Such fever may be represented by a single 'spike,' when it is generally

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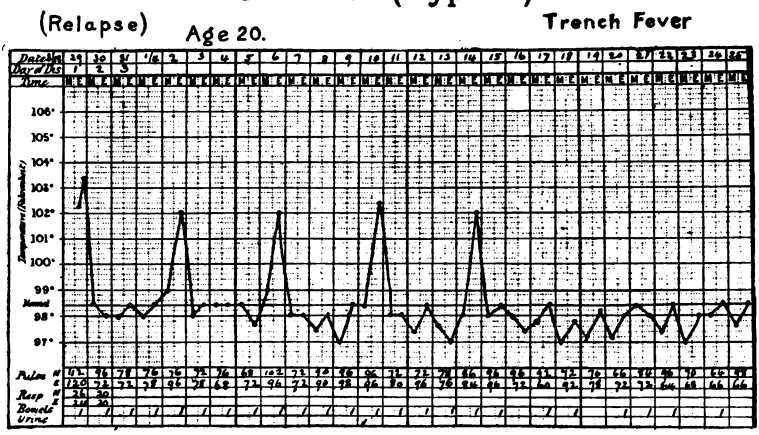
recognised as a relapse, or by a series of such spikes (Chart 8). These spikes of fever, often reaching 104° (maximum observed by us 105°), recur at intervals which are most often variable in duration, but which may give a regular periodicity of four days, more commonly five days, or longer.

The afebrile intervals usually lengthen as the disease progresses.

The history of the patient whose chart (Chart 8) is shown

CHART 8—(Type F)



as illustrating four-day fever is as follows: 'Very lousy up to July 1917, but never lousy since. Trench fever in July 1917, and in hospital continuously till November 22, 1917, having been in England since July. The first attack was a daily fever lasting for a week or more. On leaving hospital was classed as B II., and remained at duty in England till April 1918. While at duty fainted twice after unusual exertion.' While still in England, in April 1918, he was readmitted to hospital diagnosed malaria. The spleen could then be felt two fingers' breadths below the costal margin, being very definite and firm. Each rise

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of temperature has been accompanied by definite rigor. Repeated blood examinations have failed to reveal any evidence of malaria, and the administration of quinine has not modified the disease. At no time has this patient complained of pain in the bones. It is by the courtesy of Lieut.-Col. H. French, R.A.M.C., that we are able to publish this case. It would appear to be a definite instance of a late relapse, ten months after the onset of trench fever.

Of the first sixty attacks of trench fever produced by us experimentally, including both primary infections and reinfections :

18	attacks	showed	type	B	fever	=30·0 per cent.
17	,,	,,	,,	E	,,	=28·3 ,,
13	,,	,,	,,	C	,,	=21·6 ,,
7	,,	,,	,,	D	,,	=11·6 ,,
3	,,	,,	,,	A	,,	= 5·0 ,,
2	,,	,,	,,	F	,,	= 3·3 ,,

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CHAPTER II

MODE OF TRANSMISSION OF TRENCH FEVER

THAT the disease was transmissible from man to man was shown by McNee and his fellow-workers when they passed on the infection by means of the syringe, injecting the blood from a trench fever patient into a healthy man. We have confirmed this observation on six occasions. The particulars of the experiments are shown in Appendix I, Table 1, p. 152. It will be observed that the incubation period varied considerably, apparently with the stage of the disease at which the patient had arrived from whom the infected blood was obtained.

McNee further adduced evidence that the infective agent was to be found in the blood corpuscles themselves, and that even when the blood was laked the virus would not pass through a filter. Our attempts to confirm or refute this have so far proved inconclusive, for the laked blood used in Experiment 5 failed to infect though unfiltered, and therefore Experiment 6 with the same after filtration is of no value. That the blood used was originally infective is proved by the success of Experiment 4, in which the untreated whole blood from the same patient gave rise after injection intravenously to an acute and typical attack of trench fever. We can only suppose that the distilled water employed to lake the blood was sufficient to destroy the virus—a point in support of the supposition that trench fever is not a bacterial infection.

The observations of Strong and his co-workers in France

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would seem to indicate that the infective agent is free in the blood plasma, though it may adhere to the blood cells. Its filterability is not finally determined. Our own recent observations have shown that it exists in the peripheral blood during both febrile and afebrile periods up to quite a late stage in the disease (on the 51st, 79th, and 300th days of disease).

The evidence for suspecting the body-louse as the transmitter of the disease has been very conflicting in the past. We would instance the statements of Grieveson, Hurst, Weldon and Davies, Dyke, and more recently Sundell and Nankivell.

We now turn to our own attempts to transmit the disease by means of the bites alone of infected lice. In Experiment 1 an attempt was made to infect in this way, the possibility of mechanical transmission being excluded as the lice were never transferred from the trench fever patient to the healthy man until after the lapse of a period of three hours, and on only two occasions in less than six hours. Altogether the experimental subject received not less than 9518 louse bites ; the chances of infection when the various feeds upon numerous trench fever patients are taken into consideration amounted to at least 33,965. No signs of trench fever were detected in the man experimented on during a period of over two months' observation.

Experiment 2 was similar to Experiment 1 in all respects during the first 29 days of louse feeding. Thereafter no attempt was made to exclude mechanical transmission, and lice were frequently transferred from numerous febrile trench fever patients to the healthy man at short intervals, and on several occasions before the feed on the trench fever patient was complete, in the hope that the lice would continue feeding at once. Such attempts to infect were continued almost daily for 15 days. The louse

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bites totalled 13,224, and the chances of infection 52,081. This experiment gave equally negative results, though the subject was observed for over a month after louse feeding ceased, or during a period of nearly three months in all.

The lice used for these two experiments, and for all subsequent experiments in which lice played a part, were from Bacot's pedigree stock at the Lister Institute. They were kept in entomological boxes and allowed to feed, from time to time, on the various active cases of trench fever under our observation. The same lice were employed throughout these two experiments and were therefore used for quite a sufficient period of time to allow of any necessary development of the virus in them—being used for practically the whole of their lives.

While carrying out these last two experiments we were struck by the fact that neither of the experimental subjects were ever seen to scratch themselves or to show evidence of having done so. It was therefore determined to try and discover whether the failure to infect was attributable to this cause. Experiment 8 was therefore devised.

Excreta were collected from entomological boxes containing 576 lice, all of which had been fed on many cases of recent trench fever during the previous 27 days, their last feed being six hours prior to the time of collection. The excreta were obtained by tapping the boxes containing the lice, so that the powder in which the excrement results fell through the fine mesh gauze cover of the boxes, and was collected in a sterile watch-glass. For this reason the excreta obtained were thoroughly dry as far as could be observed with the naked eye. On February 5, 1918, a suitable volunteer having been obtained, a small surface of skin on the outer side of the upper arm was lightly scarified so that blood was just drawn. A portion of the collected excreta was dusted into this blood and rubbed up into a

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paste by means of a previously sterilised needle. The scarified area was allowed to dry in the air and the shirt sleeve then pulled down over it without the application of any dressing. The skin before scarification had not been treated in any way, nor had the volunteer ever, to our knowledge, been verminous or bitten experimentally by lice. Eight days later, on February 13th, a febrile illness

CHART 9

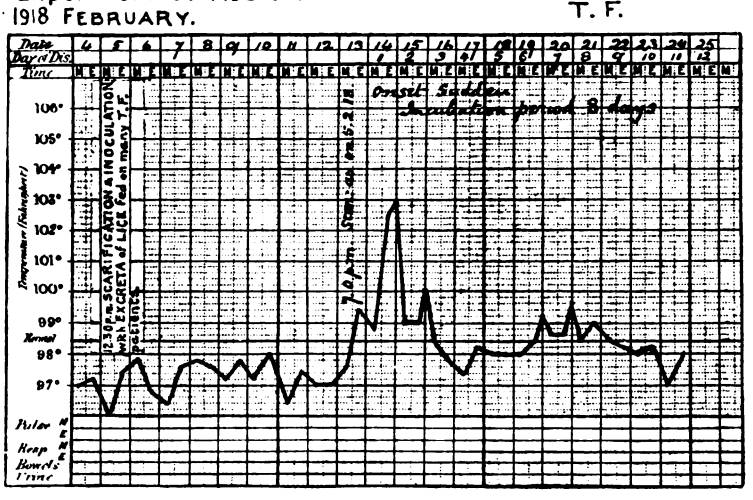

CHART 9.—The result of scarification and inoculation with excreta of lice fed on many T.F. patients.

began, which we believe was undoubtedly trench fever. A relapse followed on the 6th, 7th, and 8th days of the disease, with recurrence of symptoms, though the highest temperature recorded was only 99·6° (Chart 9). On the evening before the development of the disease a similar scarification and inoculation to that of February 5th was performed, and later the same evening the patient's temperature was found to be 99·4° though he ap-

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peared to be otherwise in his usual health. The lice from which excreta were collected for this experiment had all fed on the two volunteers used for Experiments 1 and 2, having continued to feed on them up to the day Experiment 8 was performed. The lice used for our biting experiments are therefore known to have been certainly infective.

On the same day another volunteer was scarified in like manner, and eleven lice, recently fed on a trench fever patient, were squashed over the scarified area. It seemed that such an inoculation might often take place under natural circumstances. The history of the eleven lice was as follows: From hatching they had fed daily for thirteen days (11th to 23rd day of trench fever attack) on the patient whose blood had proved to be infective on the 9th day of his disease in Experiment 4. During this period the trench fever patient's temperature was only once above normal (99°), six days before the lice were taken for this experiment. In addition, the lice received a feed on a febrile trench fever patient, whose 19th day of disease this was, fifteen minutes before their use for inoculation. No local sepsis or glandular enlargement resulted in either of these scarification experiments. After an incubation period of ten days the volunteer developed trench fever (Chart 10). The onset was somewhat gradual, though the fully developed disease was typical, with frontal headache, pain in the lumbar region and conjunctival congestion. No definite relapse occurred, though the temperature was just above normal on the evenings of the 7th and 8th days. Cardiac arrhythmia was detected for the first time on the 14th day of the disease, and then for a few hours only. Convalescence was rapid and recovery apparently complete. As in the previous experiment, scarification was repeated before the onset of trench fever: on the second occasion, three days before the onset of symptoms, sixty lice being emulsified in 1 c.c. normal saline and

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applied to the scarified area. These lice had fed twenty minutes previously for thirty minutes on two febrile trench fever patients, and all contained fresh blood when squashed.

In estimating the incubation periods in these two experiments we have disregarded the second scarification and inoculation in each case, our justification being the evidence obtained as to the incubation period in similar scarification

CHART 10

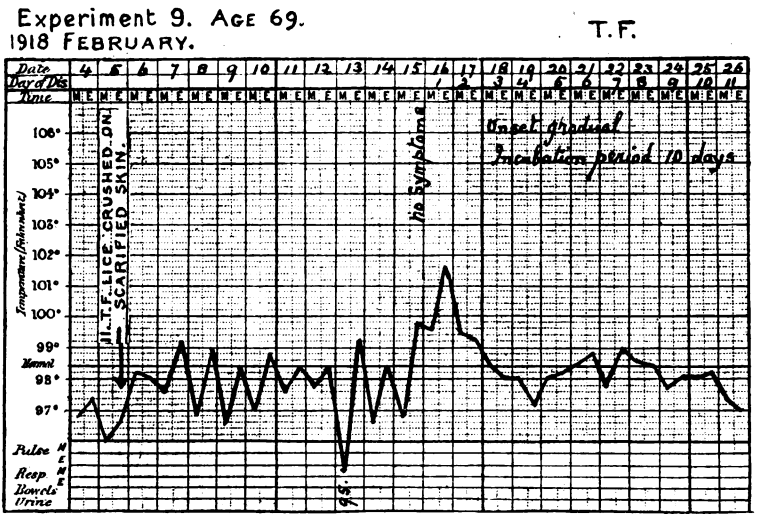

CHART 10.—The result of crushing 11 T.F. infected lice on scarified skin.

experiments performed subsequently. We have shown subsequently that 10 c.mm. of active trench fever blood, when rubbed into the scarified skin, did not produce trench fever (Experiment 38). Ten c.mm. is about the amount of blood contained by the eleven lice used in the last experiment at the moment they were squashed.

With as little delay as possible three further volunteers were obtained and inoculated with excreta from lice previously

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fed on various trench fever patients (Experiments 10, 11, and 12). These experiments were simply a repetition of Experiment 8, and all proved equally successful. In Experiments 10 and 11 the excreta were used 15 minutes after collection. In Experiment 12 the excreta were kept in a watch-glass for 1 hour and 15 minutes before use. Some of the lice from which the excreta were obtained had fed daily for the previous thirty-five days on various febrile and afebrile trench fever patients.

Of the three volunteers, the first commenced his trench fever attack, after an incubation period of seven days, by rolling out of his chair at breakfast (Chart 11). When placed in bed he complained of frontal headache, but was in such a state of mental confusion that his statements were unreliable, and his memory of this period has since remained a blank. The attack proved typical and severe, though without bone pain, and was followed by characteristic febrile relapses with a return of symptoms (Type D fever).

The second volunteer showed an entirely different onset. He became gradually ill and took to his bed, complaining of headache and vague pains in the limbs two days before his temperature rose (Chart 12). The incubation period in this case was eight days if the first rise of temperature be considered as the onset of the disease. The fully developed attack was characteristic, with frontal headache, anorexia, slight tenderness of the shins, lumbar pain, and tenderness below the right costal margin. On the following day, after a very restless night, the patient was complaining of pain below the left costal margin, and the shins were more tender. A white blood count gave 12,500 leucocytes per c.mm. By the 5th day of the disease the patient was up and feeling quite recovered. No febrile relapse followed, but later the patient felt weak and depressed, and complained of pain in the legs and region of the spleen for some weeks (Type A fever).

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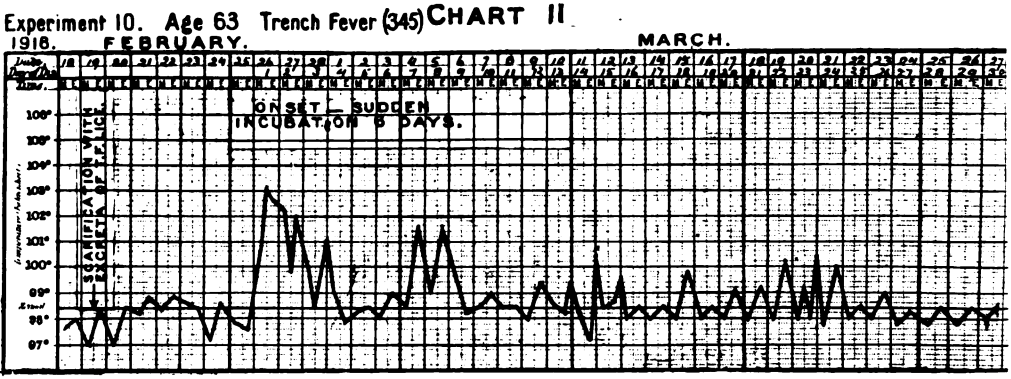

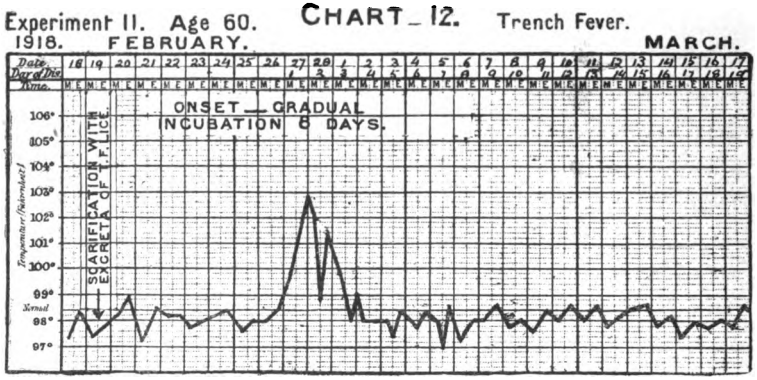

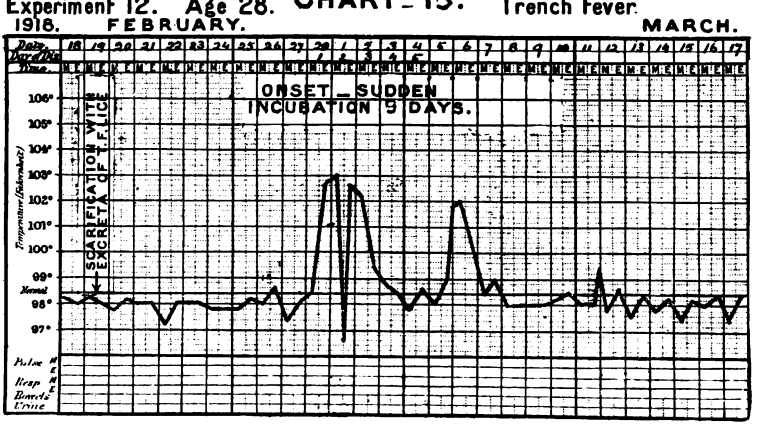

CHARTS 11, 12, and 13.—The result of scarifying and inoculating three men with one sample of T.F. louse excreta.

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The third volunteer developed trench fever after an incubation period of nine days (Chart 13). On the day of onset he was seen by one of us at noon. At that time he appeared quite fit, and his temperature was normal. After eating his mid-day meal he went out for a walk, and while out his 'legs gave way under him.' He returned home with difficulty, and, feeling cold and drowsy, lay down and went to sleep. He states that on waking he micturated freely, was nauseated, and suffering from frontal headache. When seen at 2 P.M. his temperature was already 102·6°, and the patient obviously ill.

The following day the spleen was easily palpable, but not tender. No bone, skin, or tendon tenderness could be elicited. This fever wave lasted 62 hours. After a period of apparently normal health an acute febrile relapse took place on the 6th, 7th, and 8th days of the disease. At this time the calf muscles and tendo achillis of both legs were very tender. On the 28th day of disease definite shin-bone pain and tenderness were complained of (Type C fever).

From these results it appeared obvious that the **excreta of lice fed on trench fever patients were capable, when applied to an abraded skin area, of producing a febrile illness similar in its relapsing character and general clinical picture to the disease at present known as trench fever.**

Our next Experiment (15) did much to confirm the view that we were actually producing trench fever. Five c.c. of whole blood from the volunteer infected by scarification with louse excreta in Experiment 10 were injected intravenously into a healthy man. The blood was withdrawn on the second day of disease (Chart 11). After an incubation period of five days an attack of fever developed with frontal headache, conjunctival congestion, lumbar pain, shivering, sweating, and later, pain in the shins with tenderness of the calf muscles and tendo achillis; in

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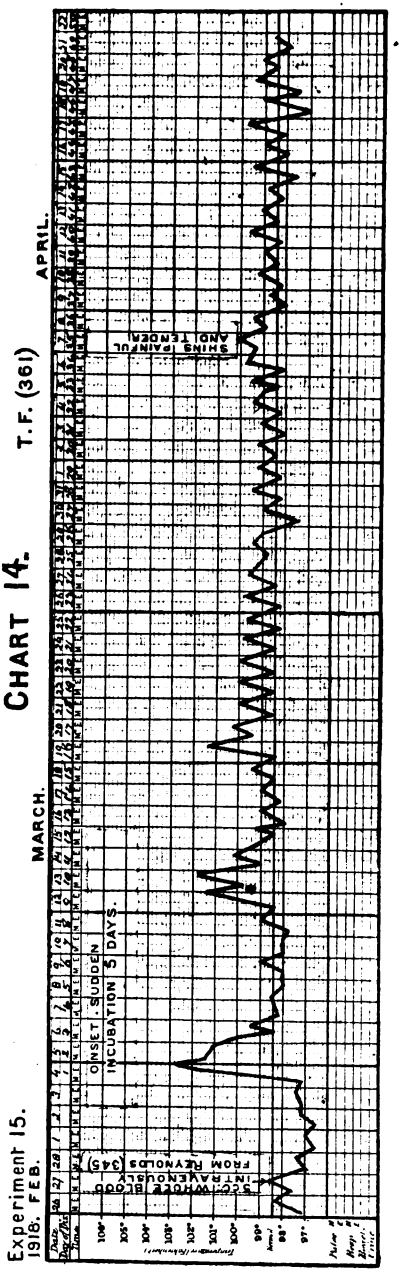

CHART 14.—The result of injecting intravenously 5 c.c. whole blood from T.F. patient, Chart 11.

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fact, typical trench fever (Chart 14). The onset of this attack corresponded exactly in point of time with the commencement of the first relapse of the man whose blood had produced the infection. Typical relapses followed.

On the same day as this whole blood transmission was performed, unfiltered serum from the same volunteer (Experiment 10) was inoculated intravenously into a healthy man (Experiment 16). The serum was obtained as follows: 21 c.c. of venous blood were withdrawn and transferred to two centrifuge tubes, no citrate being added. The blood was allowed to clot at room temperature. Three hours later the clots had fully contracted, but the serum remained tinted, and microscopical examination of a small quantity showed it still to contain blood cells. The tubes were therefore centrifugalised for 15 minutes. One tube remained slightly hæmoglobin tinted throughout, and so was rejected. From the second, 4·5 c.c. of clear straw-coloured serum were obtained, and this, 3 hours and 25 minutes after withdrawal, was injected intravenously. The volunteer remained healthy during the following 36 days' observation, and the result must therefore be considered to be negative. It seems possible that the virus we are dealing with may be capable of being thrown down by the centrifugalisation employed, so that this serum transmission experiment awaits repetition.

The foregoing experiments gave rise to the question, **Is trench fever a disease of normal lice?—Are excreta from them ordinarily infective?**

Fresh lice were therefore obtained from Bacot's stock at the Lister Institute, and the excreta collected from 500 of these during five days' feeding on a healthy man. The excreta were well mixed and rubbed into scarified skin areas of two healthy volunteers (Experiments 17 and 18). Both men remained perfectly healthy for 25 days and were

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then considered to be available for further experimental work. Our question seemed therefore to have been answered. **Trench fever is not a disease caused by normal lice,** and Bacot's stock, with which we are working, may be considered to be not infected. Cultures of the excreta used in these normal lice experiments showed what we take to be the organism of trench fever described by Jungmann. This diplobacillus would therefore appear not to be the cause of trench fever.

That excreta of lice fed on trench fever patients could infect when **recently passed** was therefore accepted. **Would such excreta retain their virulence for long periods,** was our next problem to determine.

For this purpose the remainder of the excreta, proved to be infective in Experiments 10, 11 and 12, was added to excreta collected from many other supposed infective lice. The whole of these excreta had been kept in glass tubes at room temperature, and frequently in sunlight, for 16 days. The excreta were inoculated into a scarified skin area of a healthy volunteer (Experiment 21). After an eight days' incubation period trench fever developed (Chart 15). The onset was sudden, with headache, conjunctival congestion, and the usual anorexia and thirst of fever. This fever wave lasted ten days, and was certainly suggestive of a modified typhoid attack (Type E fever). On the third day three loose brown stools containing blood and mucus were passed, but cultural and microscopical examinations of the stools for enterica and dysentery were negative. Mr. Dobell very kindly examined six stools from this patient, and reports that they were all negative for *Entamœba histolytica*. He adds that ' the only protozoa present are the encysted forms of the common colon amœba (*E. coli*), with which the patient is very heavily infected . . .' and gives as his opinion ' that the patient is not infected with *E. histolytica* ;

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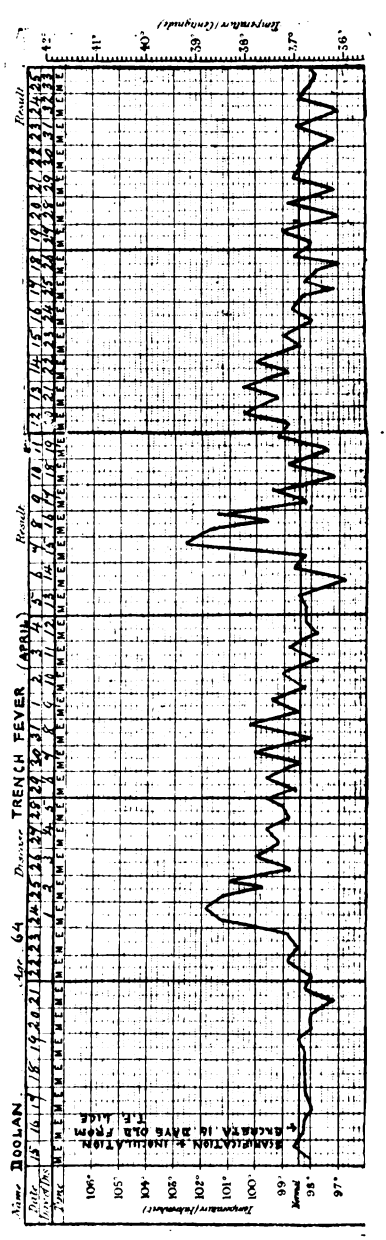

CHART. 15.—The result of scarification and inoculation with sixteen-day-old excreta from trench fever lice.

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and therefore that his attacks of "dysentery" accompanying his trench fever were almost certainly not connected in any way with this parasite.' On the 15th day of illness an acute febrile relapse commenced. The patient vomited once on the 15th day, and suffered from the same symptoms as during the first days of illness with the exception of the diarrhœa. No pains in the back or limbs and no splenic change could be detected during either initial attack or relapse. Further blood tests for enterica proved negative, and on the clinical course and temperature chart of the case we based our diagnosis of trench fever. This patient has had further intermittent fever and has developed D.A.H. Two further Experiments (57 and 95) were carried out later on the same lines, the excreta used being in part from the same sample as that used for the experiment we have just detailed, and having been kept for 60 and 120 days respectively in the two experiments. In both cases trench fever resulted from the inoculation, after 7 and 13 days' incubation. Both attacks of fever would be classed Type E, that produced by the 120-day-old excreta extending over a period of thirty-nine days. After being kept four months the excreta had required an unusually long time to incubate in the man, but otherwise appeared to be unchanged in virulence. Neither of these patients suffered from diarrhœa. How much longer such excreta are infective remains to be proved, but that **old louse excreta may be virulent without the presence of lice** must be accepted and has an important bearing on prophylaxis. Such excreta are very light when dry and can easily be blown about, so falling on abraded surfaces and wounds or into food and drink.

Could infection take place by the mouth at once became an important question. Two volunteers were therefore fed once daily, for 15 and 9 days respectively, with bread containing louse excreta which were known to be infective. At the

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same time some of the fine dry excreta were snuffed up the nostrils by each man (Experiments 13 and 14). Forty-five days later both men appeared in their usual health: this was 25 days since the last contaminated meal. In the interval one of the men had had an acute exacerbation of a chronic bronchitis, but both men had remained free of trench fever. A third man had 0·005 gramme of known infective louse excreta placed on his tongue daily for six consecutive days (Experiment 120). The excreta spread slowly in the saliva and were gradually swallowed. No effects of any kind have since been detected. We believe therefore that **trench fever is not communicable by the mouth.**

If such be a fact, the dangers to be feared from the infectivity of saliva, urine, and fæces of trench fever patients, as demonstrated by Strong, are not so great as would otherwise have been the case.

The infectivity of saliva and fæces we have not attempted to determine, but two attempts to infect with the dried sediment of trench fever urines have given negative results (Experiments 69 and 78). In the first experiment the urine was collected during the 19th to 25th days of disease, 30 c.c. being taken morning and evening each day, centrifuged and the deposit dried in an incubator at 37° C. The collected deposits were applied to a scarified skin area at one and the same time. The second experiment differed somewhat from the first, in that the urinary deposit was scratched into the skin as soon as it became dry, usually after three days, and the urine was that passed during the first ten days of an attack—ten inoculations in consequence being made. Such evidence, however, does not in any way negative Strong's findings.

Infection can, however, take place through the unbroken conjunctiva, but whether with the same facility as through

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the broken skin we do not know. In Experiment 77 louse excreta, which had been passed 24 days previously, were dropped into the lower lid once daily for three days. Eight days after the third infection trench fever developed (Chart 16), the fever curve which resulted belonging to Type B. In Experiment 119 trench fever louse excreta were dropped into the eye once only. The result was equally positive.

CHART 16

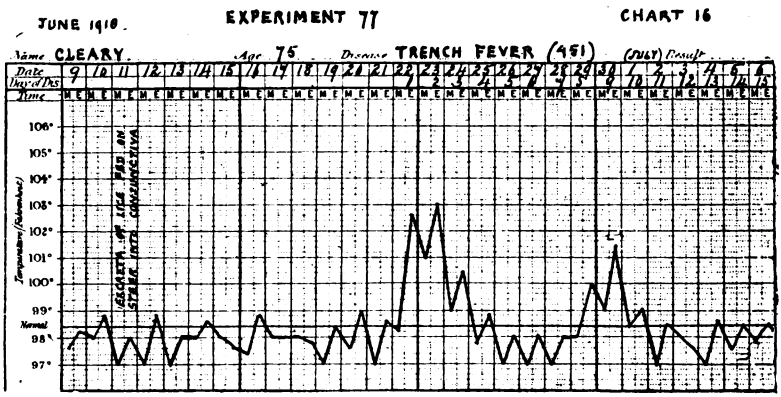

CHART 16.—The result of dropping trench fever louse excreta upon the conjunctiva.

A test for hereditary transmission of trench fever in the louse was next made (Experiment 22). Eggs were collected from boxes of trench fever infected lice. The larvæ as they hatched were placed in a clean new box and fed on healthy men. Nineteen days later, the lice being then adults, the excreta passed by them during a period of three days were collected and rubbed into a scarified skin area of a healthy man. No trench fever symptoms resulted during 26 days' observation. Two repetitions (121 and 129) of this experiment with eggs from lice whose excreta had produced six separate infections in our hands, gave equally negative results.

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We may therefore conclude that **trench fever infected lice do not transmit the virus to their offspring.**

Is the louse simply a mechanical transmitter of trench fever? or **Does a developmental stage of the virus take place in the louse?** were the next questions to be answered.

Five hundred fresh lice were obtained from Bacot's stock and placed in two clean boxes. For two days these lice were fed on healthy men and their excreta collected and retained, in order that they might be used later for control experiments if necessary. The lice were then fed five times during 24 hours on an active febrile case of trench fever whose temperature fell from 101·2° to 98·0° and then rose again to 98·6° during the period of feeding. The patient at the time was suffering from frontal headache and pains all over the body, especially in the loins and shin-bones, with later tenderness of the calf and thigh muscles. This was the 79th day of this patient's disease, he having been previously afebrile for 38 days while under observation by us. Thereafter during a period of 30 days the lice were fed only on healthy men, receiving two feeds daily and being kept in an incubator at 30° C. during the intervals between feeds. At the end of each 24 hours the lice were transferred to a new clean box, care being taken that as far as possible their excreta were not transferred with them.

Daily at the same time the excreta passed by the lice during the previous 24 hours were collected and placed in a sterile glass tube.

Owing to lack of sufficient volunteers it was not possible to inoculate men daily with the excreta so obtained. In order to cover as long a period as possible, the excreta passed during the 1st, 3rd, 5th, 8th, 12th, and 23rd days were tested by inoculation into the scarified skin of successive volunteers (Experiments 23, 24, 25, 26, 27, and 30). The excreta were inoculated each time on the day of col-

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lection, with the exception of the excreta collected on the 23rd day, which were kept for 24 hours before being used. The first four men remained healthy after inoculation for 25 days or longer.

The man inoculated with excreta collected at the end of the 12th day was the first of the series to develop trench fever (Chart 17). In this case the onset was sudden after

Chart 17

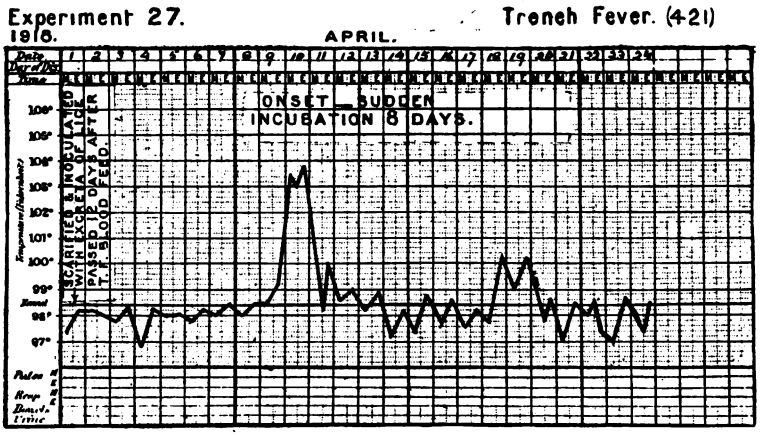

Chart 17.—The result of infection with excreta of lice passed twelve days after T.F. blood feed—the lice having fed on a healthy man only in the interval.

an incubation period of eight days. The first wave of fever lasted 72 hours, the maximum temperature attained being 103·8° on the second day. The symptoms were general malaise, frontal headache, pink eye, with later backache and tenderness of the muscles and tendons of the legs. With the fall of temperature on the third day profuse sweating occurred, and pain below the left costal arch was complained of. The pulse remained below 80 throughout the initial attack. Relapse followed (Type B fever).

The man inoculated with excreta passed by the lice during

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the 23rd day developed trench fever after nine days' incubation (Chart 18). The onset was sudden, with frontal headache, pink eye, and pain in the lumbar region, hips, and knees. The painful areas were not tender, though the patient complained of feeling so sore that he could not lie still. The temperature chart is that described as Type E fever.

Chart 18

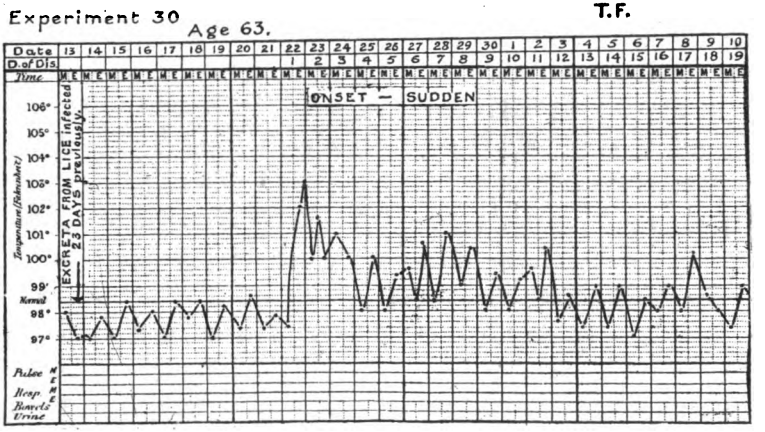

Chart 18.—The result of infection with excreta of lice passed 23 days after T.F. blood feed—the lice having fed on a healthy man only in the interval.

A similar series of experiments has lately given positive results for the 5th, 7th, 9th, 10th, 11th, and 13th days, with negatives for the 1st, 6th, and 8th. In this instance the lice received their infecting feeds on the 2nd day instead of the 79th of an acute trench fever attack, and appear in consequence to have passed infective excreta at an earlier date. Such an assumption is in keeping with the general evidence obtained by transmission and immunity experiments with blood, for in them the infectivity of the blood appears to decrease steadily as the disease progresses.

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The results of both series are shown in Table I., p. 37, and it should be noted how the incubation periods are abnormally long (16 and 13 days) in the earlier infections, indicating, we believe, that a relatively small amount of the trench fever virus is then leaving the louse, our assumption being based on the results obtained with measured doses of excreta to be discussed later.

The attack which resulted from infection with the excreta passed on the 5th day produced a fever curve which was almost identical with the one already shown as Chart 18, the result of infection with the excreta of the 23rd day.

It appears from these results that the **excreta from lice do not become infective for some days after the lice have fed on a trench fever patient, the minimum so far being five days.** Such lice continue to pass infective excreta up to the 23rd day at least while feeding only on healthy men.

To test further the resisting powers of the virus of trench fever, as it exists in the excreta of lice, a series of three Experiments (32, 33, and 34) was carried out. A large quantity of louse excreta was collected from various sources and well mixed. Some of this excreta had been proved to be infective in Experiment 21 ; all was believed to be infective. This mass of excreta was divided into four parts. The first part was bottled and kept for future work. The second part was rubbed into the scarified skin of a volunteer in equal portions on three successive days. This was a control experiment to prove the infectivity of the material dealt with (Experiment 32).

The third part was placed in a glass tube, previously warmed, the mouth of which was then closed with a plug of dry cotton-wool. The tube was immediately placed in a hot-air bath registering a temperature of 55·7° C., and kept there for 20 minutes, by which time the temperature of the bath had risen to 56·0° C. The excreta remained thoroughly

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TABLE I.—Showing Day after Infecting Feed on which Lice first passed Infective Excreta

Series.	Source of Infection.		Day after Infection of Lice on which Excreta were passed.														
	Name.	Day of Disease.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	23
1.	Gatehouse .	79	−		−		−			−				+ 8				+ 9
2.	Jones . .	2	−					−	+ 13	−	+ 9	+ 7	+ 8		a + 13			
							+ 16	−	+ 13	−								

[Small figures below + results indicate incubation periods.]

a—Reinfection.

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dry throughout. A portion was then rubbed into the scarified skin of a healthy man. The following day the balance of the excreta was reheated to 55·0° C. for 20 minutes, as there seemed some chance that the excreta had become contaminated in the interval. This reheated excreta was divided into two portions, and one rubbed into the scarified skin of the same man on that day and the other on the next (Experiment 33).

The fourth part was placed in a glass tube, the mouth of which was then closed with cotton-wool, and the tube placed in a vapour bath registering 80·5° C., and kept there for 10 minutes. The excreta became slightly moistened during the process. On removal they were divided into three portions, and these were rubbed into the scarified skin of one healthy man on each of three successive days (Experiment 34). This degree of heat was employed as sufficient to destroy a virus other than a spore-bearing organism. 56·0° C. for 20 minutes was employed in the previous experiment as being the temperature of dry heat necessary to disinfest clothing.

The man inoculated with the unheated excreta developed trench fever after an incubation period of 8 days (Chart 19). The onset of the attack was sudden, with frontal headache, pain in the muscles of the thighs and left arm, shivering, sweating, a marked leucocytosis, and later lumbar pain. A febrile relapse followed on the 6th, 7th, and 8th days, during which definite shin-bone pain was complained of in both legs. No tenderness, however, was elicited.

Vertigo was complained of in the interval between these two febrile waves.

The repetition of the inoculation in this case made no apparent difference in the course of the disease or the temperature curve. The chart of the case is shown with the two-hourly observations that we are in the habit of making, and illustrates the rapid fluctuations of temperature, pulse-

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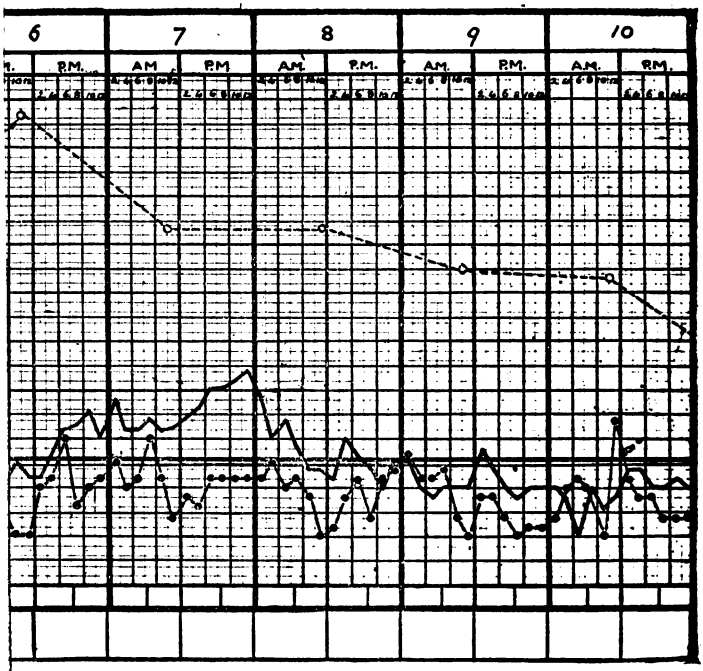
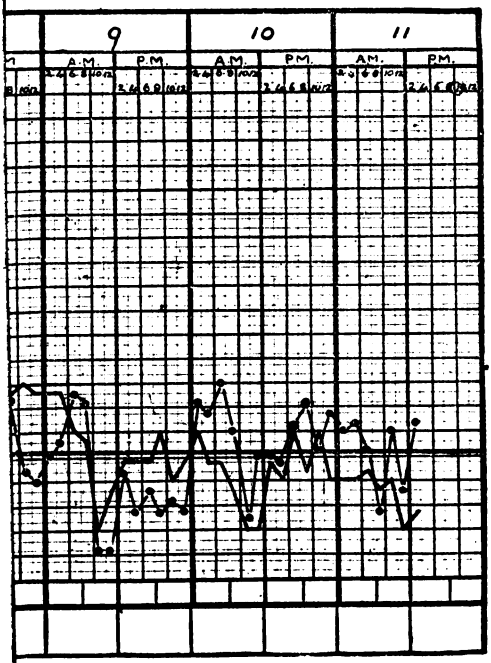
T.F.364.



T.F.380.



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rate and leucocytosis which are so characteristic of the febrile stages of the disease. The gradually mounting leucocyte count during the last four days of incubation is well brought out.

The excreta heated dry to 56·0° C. proved equally virulent. After an incubation period of 8 days the volunteer developed trench fever (Chart 20). The onset of the attack was sudden, with frontal headache, slight pink eye, and a moderate leucocytosis. A febrile relapse, with the same symptoms, followed on the 6th, 7th, and 8th days, with a second relapse commencing on the 12th day. The whole attack was mild, without limb pains, but otherwise characteristic. His disease was passed on to others both by the syringe and by lice.

The man inoculated with the excreta heated moist to 80·5° C. remained healthy. Such a temperature must therefore be considered as sufficient to destroy the trench fever virus, which is in consequence not a spore-bearing organism. The lowest temperature required to disinfect as well as disinfest the clothing of trench fever patients will be dealt with in the chapter on ' Prophylaxis.'

Having determined that the excreta from lice fed on an active trench fever patient were constantly infective for man, if collected at the right time, it now seemed advisable to ascertain **what percentage of lice passed such infective excreta.** From clinical histories it appeared that ' two or three lice ' had not infrequently been sufficient to infect a patient. If such a high percentage of lice became infective as these statements suggested, the careful microscopical examination of a small number of lice might be expected to be sufficient to reveal evidence of the infecting organism should it be demonstrable. Ten clean lice were therefore fed twice daily on an active febrile case of trench fever for a period of 18 days. The excreta passed during the

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last three days of that time were collected and inoculated into a scarified skin area (Experiment 60). Trench fever resulted after an incubation period of nine days (Type B), the onset being sudden and pain moderately severe during the relapse.

Meanwhile the lice had been separated into two parties of five each, and fed as usual on the same patient. The excreta passed by one batch of five were collected during the next seven days, and inoculated into the skin of a volunteer (Experiment 66). Trench fever again resulted, the incubation period being reduced to seven days, and the fever wave prolonged to twenty-seven (Type E). Two lice only of this same batch of five continued to live and thrive; both were females and appeared healthy. For some time past the individual lice had been housed separately in glass tubes and kept in an incubator at 32° C., being placed on the skin of the arm twice daily for feeding purposes.

The excreta passed by one of these lice, from the 26th to 31st days from the commencement of infection, were collected and inoculated (Experiment 71); from the other, those passed from the 27th to 32nd days were dealt with similarly (Experiment 79). The excreta of both lice proved to be infective, the two volunteers developing trench fever after eight and nine days respectively.

The fever which resulted in the first of these single louse infections was severe (Chart 21), though short in duration, and was accompanied by severe frontal headache, shivering, marked pink eye, pains in the back and thighs, and intense shin pain within six hours of the onset. No symptoms of any kind were complained of after the 6th day of the disease, but it is obvious that **one louse may produce a severe and typical attack of trench fever.**

It may also safely be said that **a high percentage of lice become eventually infected while continuing to feed on a**

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trench fever patient. Exactly what the percentage is we are not in a position to say, and we would leave our readers to

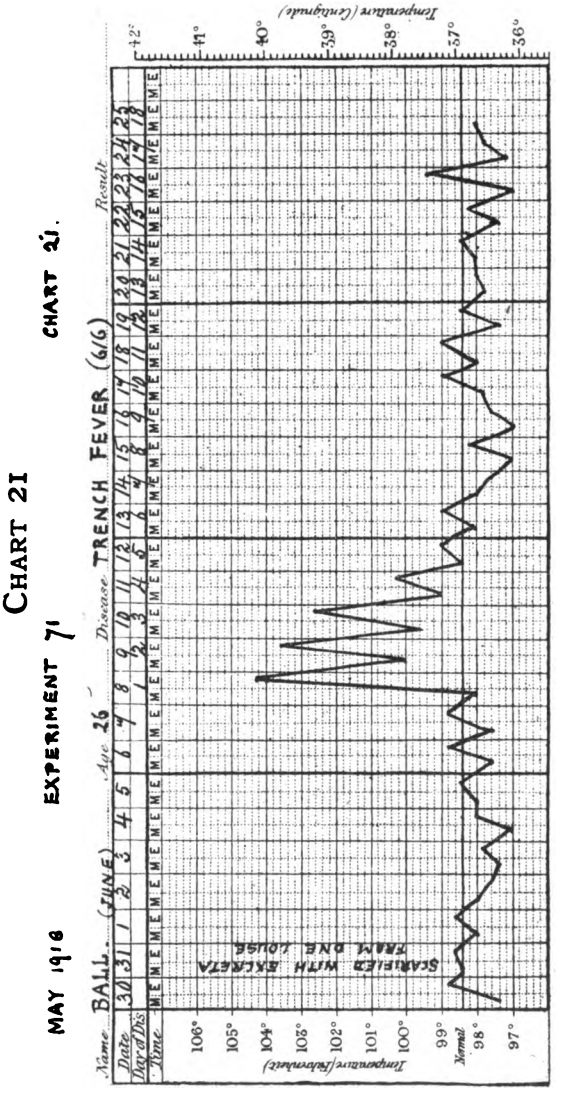

CHART 21.—The result of infection with excreta passed by one louse during five days.

deduce what they may from the data we have given. In any case it is obvious that the microscopical study of single

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lice, during the third week from infection, may be profitably undertaken.

Experiment 79 resulted in a Type C fever and a prolonged convalescence.

That the clinical attacks in these four experiments should have varied so greatly is of importance when it is remembered that the lice which produced them had all fed on one and the same patient, for it is therefore necessary to suppose that the differences resulted from individual peculiarities in the men infected or from variations in the size or virulence of the doses they received.

We hope to show that both factors play a part, for in these two single-louse infections, the number of lice, the amount of excreta, and the days from original infection of the lice were almost the same, only the men themselves differed. The one whose chart is shown, and who was convalescent on the 6th day, was aged 26, and obviously robust, while the other (Experiment 79), whose convalescence was prolonged, was aged 54 and, though healthy, of poor physique—the result of nasal obstruction.

That dosage may play an important part in the type of attack produced is strongly suggested by the following observations.

When infections were produced by the application of louse excreta to the broken skin, it was realised that much of the excreta employed never came in contact with the body fluids, and that therefore the dosage required to infect could not be studied by this method of infection. If louse excreta could infect when introduced subcutaneously it would be possible to ensure that the whole quantity used for an experiment actually reached the body fluids, and the amount of excreta required to produce infection could then be studied. An emulsion of infected louse excreta was therefore made in normal sterile salt solution. The

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excreta had been previously freed of gross debris and then carefully mixed, having been passed by lice which had fed on an active recent case of trench fever from eight to twenty-two days previously. The excreta used in making the emulsion was carefully weighed, and the amount contained in each cubic centimetre was probably equal. Three volunteers were inoculated subcutaneously with this emulsion within one hour of its preparation. The first received an amount equivalent to 2 milligrams of excreta (Experiment 96), the second 0·1 milligram (Experiment 97), and the third 0·05 milligram (Experiment 102). The first two men developed trench fever, so proving that **louse excreta can infect when introduced subcutaneously;** the third remained healthy while under observation during twenty-five days.

A study of the two temperature charts (22 and 23) of the successful infections reveals essential differences. The larger dose (2 milligrams) produced a fever wave lasting ten days with no afebrile intervals; the smaller dose (0·1 milligram) produced a Type C fever with definite afebrile intervals; in fact, a 'spiky' chart. The incubation periods were also noticeably different, being seven days with the larger dose and eleven days with the smaller. It seems, therefore, that **in the size of the infecting dose we may have an important determining factor for the type of fever produced.** That many individuals who received equal doses of the same sample of excreta would all react similarly is improbable, as the individual peculiarities of each would play a part; but when each receives what is for him the minimal infecting dose, it is possible that the febrile reaction will resemble that shown in Chart 23. In this case, resistance was apparently developed quickly with a resulting rapid fall of temperature but without lasting immunity, as shown by a recurrence of fever after an interval equivalent

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CHART 22

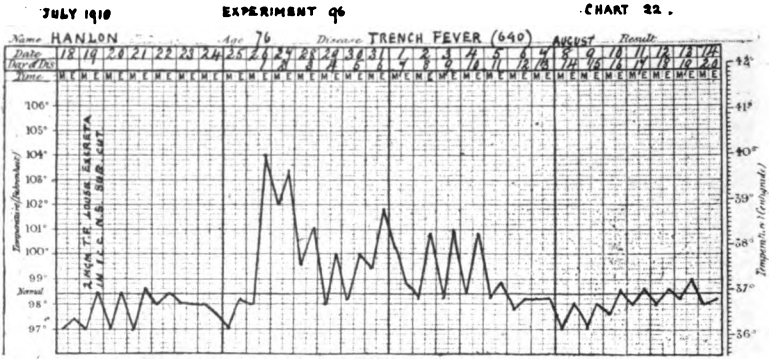

CHART 22.—The result of the subcutaneous injection of 2 mgm. of louse excreta.

CHART 24

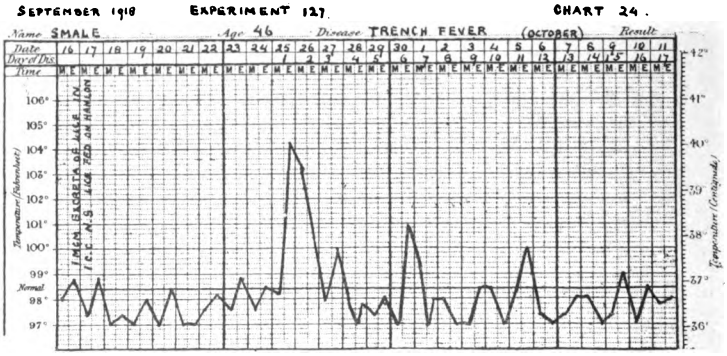

CHART 24.—The result of the subcutaneous injection of 1 mgm. of louse excreta.

CHART 23

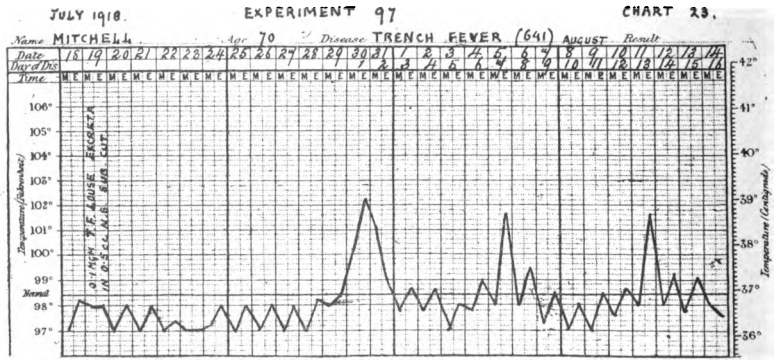

CHART 23.—The result of the subcutaneous injection of 0·1 mgm. of louse excreta. 0·05 mgm. of this same excreta failed to produce infection. Note the increasing incubation periods as the dose was reduced.

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to the shortest incubation period produced by infection with blood.

Similar febrile reactions are frequently seen in reinfected men, and in those who relapse after long afebrile intervals; the explanation in each instance is probably the same—immunity sufficient to deal quickly with the amount of toxin liberated at a given time.

Our third experimental patient in this series probably received what was, for him, a subminimal dose, as the number of persons naturally and absolutely immune is apparently extremely small. This case will be discussed in the chapter on 'Immunity.' The exact determination of the minimal infecting dose of louse excreta is probably impossible, as it nearly certainly varies for different individuals, and samples of louse excreta from different sources of infection, or after different periods from the infection of the lice, will vary in their relative infectivity. We have already seen how excreta passed by lice within five days of their infection are apparently non-virulent for man, and how, after the fifth day, the infectivity of the excreta, as estimated by the decrease in the incubation period required in the man inoculated with them, increases steadily.

Up to this point our knowledge of the infectivity of the blood was confined to two facts—(*a*) the blood of a trench fever patient is capable of infecting both man and louse while the patient is febrile, and (*b*) the blood of a febrile patient as late as the 79th day of disease is capable of infecting lice.

Is the blood infective during an afebrile interval was a question of importance.

A suitable patient having been found (Chart 25), lice were fed on him on the evening of the 27th day of his attack (temp. 97·7°—98·2°) and again on the 28th morning (temp. 98·4°—98·4°). As will be seen by the chart, his

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CHART 25

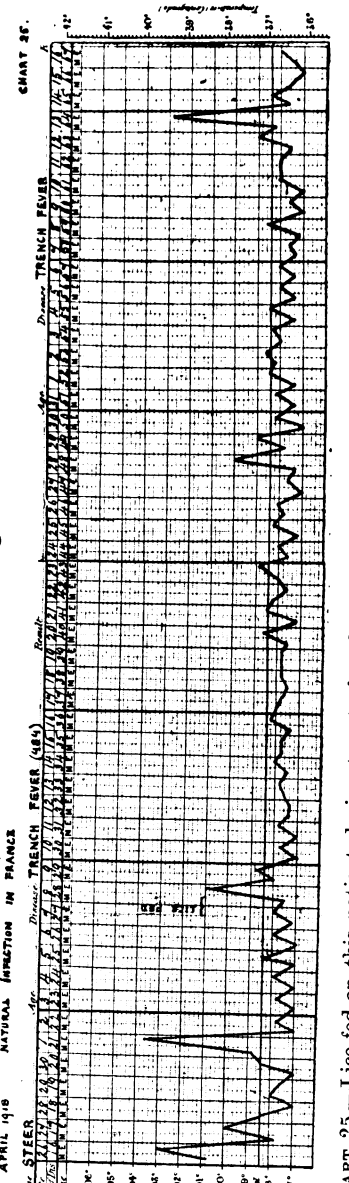

CHART 25.—Lice fed on this patient during twenty-four hours while he was afebrile, and excreta from them produced the infections shown as Charts 26, 27, 28, 16, and 29. This man contracted his infection under natural conditions in France.

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temperature rose again on the evening of the 28th day to 101°, but while the lice fed the patient was strictly afebrile, so that the lice only fed during an afebrile interval. Thereafter the lice were fed on a healthy and afebrile man who had never been exposed to infection with trench fever.

The excreta passed by the lice eleven, twelve, and thirteen days later were collected, and with them we successfully infected seven men (Experiments 64, 70, 73, 75, 77, 81, 84), thereby proving that **the organism of trench fever is present in the peripheral blood during the afebrile intervals.** The charts of five of these men (Charts 26, 27, 28, 16, and 29) are reproduced, and it is interesting to note the dissimilarity of a series of fever curves produced from a single source of infection, and that infection of an undoubted 'spiky' type (F) can and does produce the other types of trench fever. In fact, that **the various types of trench fever are one disease, not many.**

CHART 26

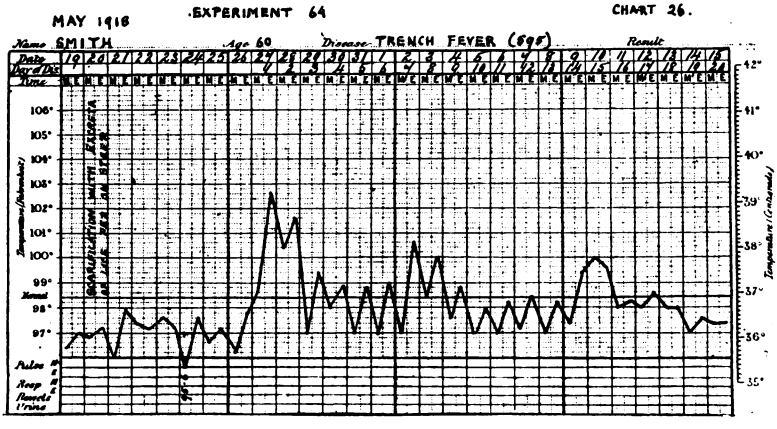

CHART 26.—The result of infection with excreta from lice fed on a trench fever patient while afebrile only.

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CHART 27

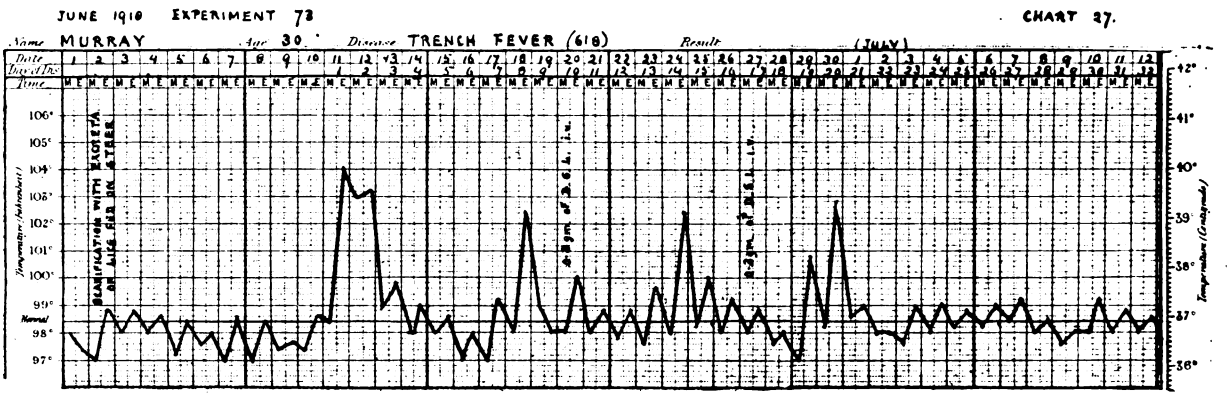

CHART 27.—The result of infection with trench fever louse excreta heated dry for twenty minutes at 68·2° C. to 70° C. (See Chapter viii., 'Prophylaxis.')

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CHART 28

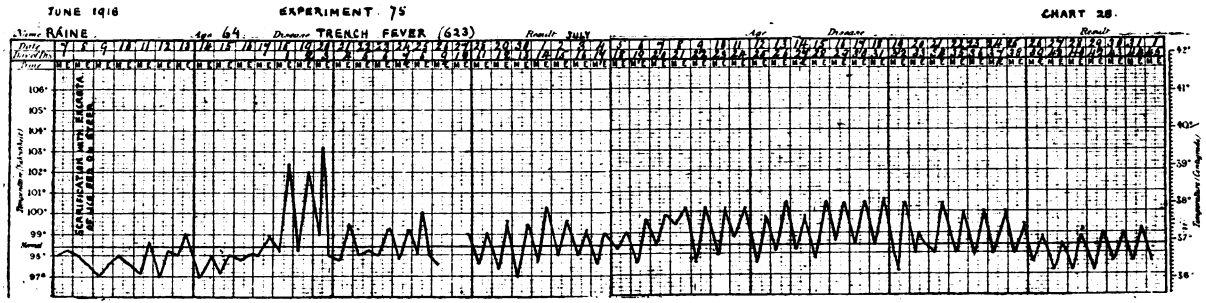

CHART 28.—The result of infection with trench fever louse excreta soaked in soap and hot tap-water for twenty minutes.

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CHART 29

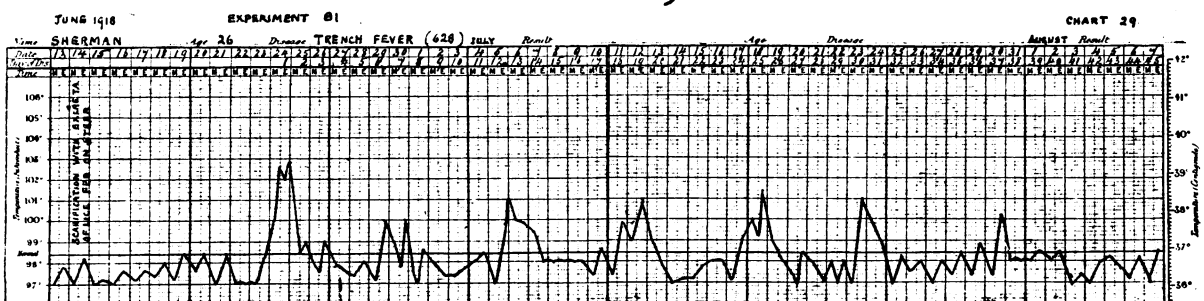

CHART 29.—The result of infection with finely ground trench fever louse excreta.

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The incubation periods of these seven infections were 7, 8, 9, 10, 11, 10, and 8 days, in that order. The two patients whose incubation periods are recorded as ten days, however, each suffered from definite prodromal symptoms—headaches and nausea in one case, and headaches in the other—for two days before their fever began, so that their incubation periods may practically be considered as eight days each. The patient whose incubation period was 11 days was infected through the conjunctiva, and therefore should be omitted from the present consideration.

It will then be seen that six infections produced by inoculation into the broken skin of one sample of louse excreta of presumably uniform infectivity—for it was well mixed before being divided—gave uniform incubation periods of between seven and nine days. This, again, we consider to be evidence that the incubation period varies with the infecting dose and supports the contention, which we have already advanced, that the long incubation periods (16 and 13 days) following inoculations with excreta passed by lice in the early days after their infection (Table I.) indicate that **the number of the trench fever organisms passed by the lice increases as the time from the infecting blood feed lengthens.**

In other words, that lice pass but few trench fever organisms up to five days from the time they first feed on trench fever blood, an increasing quantity after six, seven, and eight days, and after this, so many, that their excreta contain a maximum infecting dose in quantities of two milligrams upwards.

That the explanation of the shortening incubation periods is not an increase of virulence of the organisms passed is suggested by the incubation periods being lengthened as the dose of excreta, of uniform virulence, is reduced in weight. (Experiment 96—incubation 7 days with 2 mgm.

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of excreta. Experiment 97—incubation 11 days with 0·1 mgm. of the same excreta.) No quantity of the most virulent excreta—and we have inoculated as much as 32 milligrams into a single individual—seems capable of reducing the incubation period to less than seven days.

We may say, therefore, that **the incubation period of trench fever is seven to nine days, when infection is produced through the skin by means of a maximum dose of infective louse excreta, with periods increasing to sixteen days as the infecting dose is reduced.**

A consideration of the incubation periods in all our experimental infections with louse excreta by this route supports this statement.

Our two infections with excreta in the conjunctival sac gave incubation periods of eleven and twelve days.

Having settled that an acute case of trench fever, whether febrile or not, is capable of infecting lice, it became essential to know how late in the disease lice could become infected. Many patients continue in ill-health for months after the acute febrile stage is past, some of them relapse with marked fever from time to time, whilst others pass into a condition which is variously labelled as myalgia, neurasthenia, or D.A.H., as one or other group of symptoms attracts most attention, without there being sufficient fever to indicate the origin of the trouble. Many such sufferers have returned to civil life, many more mix freely with their comrades in the army. Are they 'carriers' and a danger to their fellowmen, or, worse still, to their children?

To obtain evidence on this point, three hundred lice from Bacot's stock were fed twice daily on a patient part of whose acute attack we had witnessed and who had been under our observation for nearly nine months. The lice were fed twice daily from what we estimated to be the 298th day of disease till the 339th day, the excreta passed by

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them from the 11th to 24th days of this feeding being collected. During this time the patient's temperature rose to 99° six times in the evening, and the pulse rate, at rest, frequently to 100 (Chart 30). He complained of indefinite pains in the limbs, a tendency to excessive sweating, the symptoms of disordered action of the heart, and was nervous, depressed, and much below his normal weight. An eminent neurologist examined him for us at this time, and reported on him as follows :

'Age 28. Married four years, and in civil life was manager of a large dairy business. He gives his history as having joined up in December 1916, going out to France in May 1917 and joining the Household Guards. He served at Arras, but was never wounded or buried. He was once "blown up" but was never unconscious, although he suffered from "shock" for about an hour. In July 1917 he was sent home with trench fever and admitted to Hampstead Hospital, and has been there since.

'He complains of insomnia ; cannot "get off" to sleep ; once he does, he sleeps restfully. No dreams.

'**Physically.**—Superficial and deep reflexes react readily and excessively. Marked tremors—more so on right side. No loss of sensation. Some slight inco-ordination, most marked in the upper limbs. Tongue furred. States he has no appetite and cannot eat meat. Heart's action rapid and tumultuous. His writing is shaky, especially down strokes. Pupils react : perimeter field contracted above and below.

'**Mentally.**—States he has no energy to do anything, complains of headache, feels "nervous" and that he must scream out. He states he has a dizzy feeling in the head, and that he is going off in a faint, this feeling being especially marked when he is in the Tube or in some closed space. He finds he has to gasp for breath, and this feeling may come on suddenly at night, when he wakes up perspiring freely.

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He is emotional as he relates his history, and thinks he will not be of further use and will not get well, but is brighter when reassured. **He is suffering from neurasthenia.'**

The collected louse excreta were then applied to the scarified skin of a healthy volunteer (Experiment 72). Ten days later this man complained of general malaise and

CHART 30

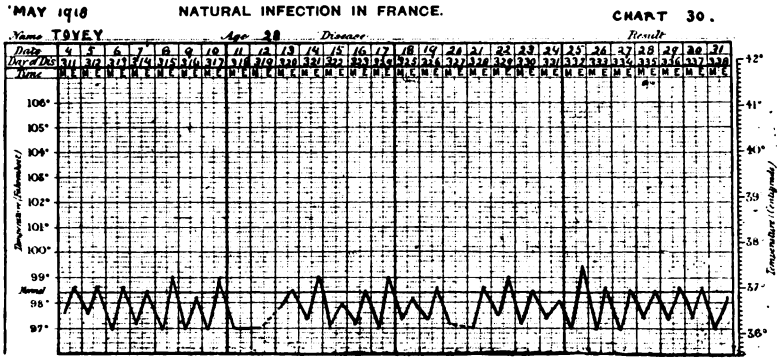

CHART 30.—Patient said to be a neurasthenic. Lice were fed upon him from the 298th to the 339th day from the onset of his trench fever attack. During this period he was only febrile as shown. The excreta from these lice produced the infection shown on Chart 31.

CHART 31

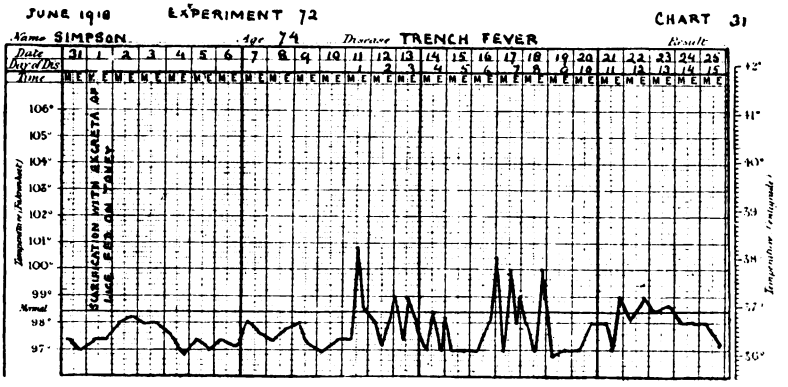

CHART 31.—The result of infection with excreta from lice fed on the neurasthenic patient whose chart (30) is shown above.

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CHART 32

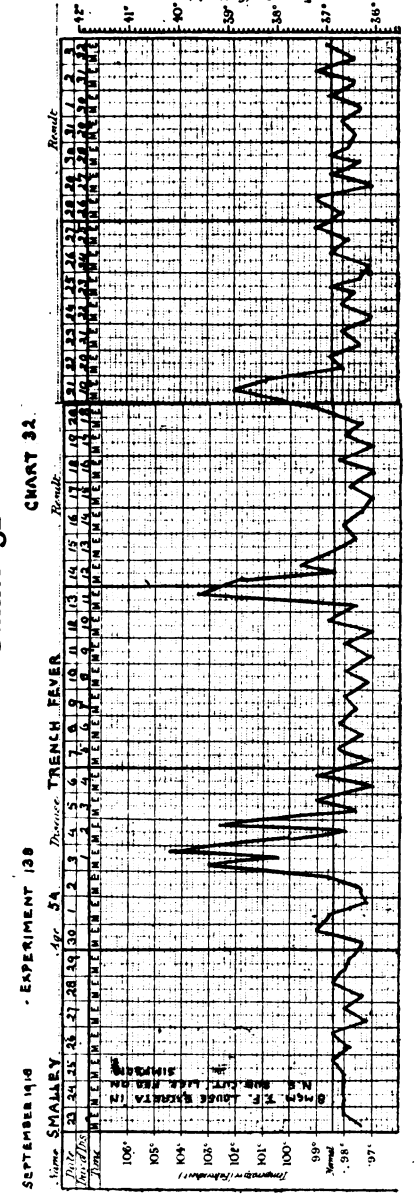

CHART 32.—The result of infection with excreta from lice fed on the man infected from the neurasthenic case.

The three charts seem to indicate that the virulence of the infection has been enhanced by a series of passages through man and louse, and that even old chronic cases of trench fever are a danger to their associates if they are lousy.

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backache, with later pain in the lumbar region and legs, and frontal headache. His eyes became pink, and later in the day his temperature rose (Chart 31). A relapse followed on the 6th, 7th, and 8th days, and a second on the 11th and 12th, after which recovery was rapid. During this fever period lice were fed on the volunteer, and excreta from them inoculated into a healthy man (Experiment 138). Chart 32 shows the result.

It can only be supposed, therefore, that this case of 'neurasthenia' was really one of trench fever in a form capable of infecting lice and a danger to those around him.

It is obvious, then, that **the sequelæ of trench fever are but a continuance of the disease and evidence of a persistence of the infection**—a finding that must have a far wider bearing on medicine generally than in the field of trench fever alone.

While these various experiments with the excreta of lice were in progress, further attempts were made to transmit trench fever by means of the bites alone of infected lice.

Having determined that lice did not pass infective excreta for a period of from five to twelve days after an infecting feed, lice whose excreta were known to be infective were henceforth selected for these experiments.

Our first two biting experiments have already been briefly described, and evidence adduced that the lice used for them were actually infective. It should be added that our method of conducting our biting experiments has been to feed the lice on the various active cases of trench fever in our wards, whenever the patients were febrile, and in the intervals to feed the lice upon the healthy men we were attempting to infect. At the same time, excreta from the lice were collected and used for inoculation in connection with other investigations, by which means the infectivity of the lice was always proved. In Experiment 40 the man bitten was aged twenty-eight, and suffered considerably

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more irritation from the lice than the two old men used for our original experiments. The lice fed on him through the chiffon covers of the entomological boxes, several hours always intervening between a feed on a trench fever patient and on the volunteer. No attempt was made to clean the skin after feeding. 4945 bites were received during a period of seventeen days, and the volunteer observed for forty days. No evidence of trench fever resulted.

In Experiment 47 the man bitten was aged forty-four. Lice were fed on him twice daily for fourteen days, during which time he received over 23,000 bites. For feeding purposes the lice were liberated on the skin, and no attempt was made to remove the excreta passed while they fed. We observed the man for twenty-two days, he being unable to remain with us longer, and no trench fever resulted. The lice used were undoubtedly infective, as they were also used for the next experiment, the boxes being frequently interchanged between the two men.

In Experiment 48 the man bitten was aged fifty-four. The lice fed on him through chiffon, and their excreta were always carefully wiped off the skin by means of dry cotton wool immediately after each feed. This man did not scratch himself as far as could be observed, and after receiving some 25,000 infective bites, during fourteen days, he developed trench fever. His attack was severe and typical, with recurrent pyrexia, lasting thirty-nine days. His spleen became distinctly palpable for the first time on the 15th day of disease.

In Experiment 50 the man bitten was aged twenty-nine. The lice fed twice daily on him through chiffon for a period of fourteen days, and nearly 22,000 bites were received. The infectivity of the lice was proved by inoculation of their excreta. During fifty-nine days' observation the volunteer remained free of trench fever.

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In Experiment 67 the man bitten was aged twenty-eight. The lice fed twice daily through chiffon for five days. The skin was washed with absolute alcohol directly after louse feeding on each occasion; intense irritation resulted: 7500 bites were received, and the man was observed for thirty-one days, during which time he remained perfectly healthy.

In Experiment 68 the man bitten was aged twenty-one. The lice fed through chiffon for thirty-two days, the skin always being washed with absolute alcohol after louse feeding. Over 40,000 bites were received, and on the 35th day from the commencement of the experiment trench fever developed. The attack was mild, and followed by one short relapse (maximum temperature 99·2°), the patient being convalescent by the 10th day. In this case the skin irritation was quite moderate and had not resulted in scratching.

It will be seen, therefore, that in eight louse feeding experiments, two infections with trench fever had been produced—25 per cent. positive results. (Table II.) The degree of louse feeding had been intense, and the most

TABLE II.—Louse Feeding Experiments

Experiment Number.	Name.	Number of Days over which Feeding extended.	Number of Bites.	Result.	Incubation Period (in days).	Period of Observation after Louse Feeding began (in days).
1	Cole . .	35	9,518	–	...	73
2	Edgeler .	41	13,224	–	...	67
40	Riches .	17	4,945	–	...	40
47	Prince .	14	23,821	–	...	22
48	Jackson .	14	25,609	+	14	57
50	Bell . .	14	21,908	–	...	59
67	London .	5	7,520	–	...	31
68	Barnett .	32	40,580	+	35	65

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heavily infested man can seldom be bitten by lice in such concentration as we employed. These facts should be contrasted with the clinical evidence that 'one or two lice' have been sufficient to produce infection; with our experimental evidence that the excreta from a single louse, when inoculated, may cause trench fever (Experiments 71 and 79); and that the gut of a single louse applied to a broken skin surface is sufficient to produce an acute attack. (Experiment 101.)

The contrast between the incubation periods when infection is produced by biting and by inoculation with excreta is even more remarkable.

Bites may eventually cause infection after very varying periods which range from fourteen days to as many weeks, according to the evidence of German investigators. With the rubbing in of excreta the incubation periods are almost constant, from seven to nine days, being slightly lengthened as the dose is reduced. The percentage of infections resulting from the two methods shows that when inoculation with excreta is employed infection nearly inevitably results, whereas, when infected lice bite a man, trench fever has never resulted in more than 76 per cent. of the cases, and then usually under distinctly abnormal conditions. (Osler, *Lancet*, 12.10.1918.) Our own series of biting experiments only gave 25 per cent. positive results.[1]

We are of opinion, therefore, that trench fever is conveyed by the excreta of infected lice; that the excreta may enter through the broken skin or unbroken conjunctiva; that rubbing and scratching promote infection, but that the bites of lice may possibly cause a sufficient lesion to enable the virus to enter the body.

In this connection we may mention that lice are constantly

[1] For further evidence that infection by the bite is accidental, see Appendix.

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contaminated with their own excreta, masses of which may be seen by means of a hand lens adhering to their surface, and that, no matter what position lice are fed in, their excreta will be found to reach the skin on which they are feeding, and often in a semi-fluid condition as the result of solution in the sweat.

We may add here that one attempt we made to transmit trench fever by means of the bed bug gave a negative result (Experiment 113). In this experiment both bugs and their excreta were emulsified and injected subcutaneously.

Finally, our efforts to transmit the trench fever virus by means of blood applied to the scarified skin may be reviewed.

Three experiments were performed and all with equally negative results. In the first (Experiment 38), 10 c.mm. of venous blood from an active trench fever case, on the second day of disease, was smeared on the skin and scarification performed through it at once. The infectivity of the blood at the moment was proved by control (Experiment 36). In the second (Experiment 44), 1 c.c. of the same blood, taken at the same time, was dried at room temperature, and eight days later the whole of it applied to a scarified skin area.

Our Experiment 87 has shown that 0·5 c.c. of venous blood when injected intravenously, after citration, is a sufficient quantity to infect. In the third experiment (88), 0·5 c.c. of venous blood was smeared evenly over the whole surface of the anterior aspect of the forearm, and extensive light scarification performed through it while still wet. The infectivity of this blood was proved by Experiment 87. It is possible that the amount of blood employed in each of these experiments has been insufficient, the whole amount used certainly not coming in contact with the body fluids.

A comparison of the clinical features of our experimental infections is of some interest. Of the sixty attacks of trench

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fever produced by us, three-quarters have been sudden in onset and the rest gradual. The majority after discharge from hospital have returned to some form of useful work. Figures on this point are of no value, as many of the men were not in the habit of working when they came to us and continued their usual life on leaving hospital.

The three outstanding features are :

(1) That one sample of louse excreta in Experiments 10, 11, and 12 produced three different clinical attacks of trench fever. Two were sudden in onset and one gradual. One case showed splenic enlargement without pain, one splenic pain without enlargement, and one no splenic involvement. This last man had no pain in his limbs at any time. The other two had recurrent pains in the shin-bones. One of these had a single wave of pyrexia, the other two had definite febrile relapses. The only features common to all three were an initial fever of roughly three days' duration, with frontal headache and conjunctival congestion.

(2) That the blood from the case without limb pains, just noted, when injected intravenously into another man, produced an attack of relapsing trench fever with marked shin-bone pain.

(3) That lice fed on a single case of trench fever (Type F) produced infections showing the varying types of temperature curve associated with the disease. (Experiments 64, 70, 73, 75, 77, 81, 84.)

The majority of the attacks can only be described as mild, the patients making an uninterrupted recovery in about three weeks. Such a course is that probably followed by the majority of natural infections in France and elsewhere, provided that the men are otherwise healthy when they contract the disease and that they are put to bed without delay when symptoms first appear.

A recent experiment (151) has shown that **the head louse**

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(*P. capitis*) **is capable of conveying the disease in the same way as the body louse** (*P. corporis*).

The evidence obtained from our experimental work thus far may be summarised as follows :

(1) The whole blood from febrile trench fever cases, up to the 51st day of disease, when injected intravenously, is capable of reproducing the disease. The incubation period in such infections varies greatly—from 5 to 20 days.

(2) The virus as contained in the circulating blood may be destroyed by the addition of distilled water in large quantities.

(3) The excreta of infective lice (*P. corporis* and *P. capitis*), when applied to a broken skin surface, readily produce trench fever. Rubbing and scratching promote the introduction of the excreta, but the lesions caused by the bites of lice may possibly be sufficient to allow of its entry. The incubation period in such infections is remarkably constant and averages eight days.

(4) The excreta of infective lice readily infect when placed on the conjunctiva.

(5) The excreta passed by lice fed on trench fever patients are not infective till the expiration of not less than five days from the commencement of the feeding on trench fever blood, thus indicating a developmental cycle in the louse, or a period during which the organism multiplies.

(6) Once lice are infective they remain so till at least the 23rd day from the date of their infection.

(7) A very high percentage of lice eventually become infected while continuing to feed on a trench fever patient.

(8) The excreta from a single louse, or its gut contents, are capable of producing trench fever.

(9) 0·1 milligram of infective louse excreta has produced typical trench fever by inoculation subcutaneously; 0·05 milligram of the same excreta failed to do so.

(10) The virus of trench fever, as contained in infected

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louse excreta, is capable of withstanding drying, exposure to sunlight, and keeping for at least 120 days.

(11) The bodies of infected lice when crushed upon the broken skin are capable of producing trench fever. When lice become so infective remains to be determined.

(12) Active trench fever blood does not produce trench fever when rubbed into the broken skin.

(13) Lice can be infected on an afebrile trench fever patient while the disease is still active.

(14) Infection probably does not take place by the mouth or by inhalation.

(15) The excreta of normal lice are not capable of producing trench fever.

(16) Trench fever infected lice do not transmit the disease to their offspring.

(17) The percentage of individuals naturally immune to trench fever is exceedingly small.

(18) Old age is no bar to infection.

(19) Even as late as the 300th day of disease a patient's blood may remain infective, and be capable of infecting lice fed on such a patient while slightly febrile.

(20) The different varieties of trench fever result from differences in the persons infected rather than in the source of infection, though dosage may play an important part in the type of attack produced.

The men on whom these experiments have been performed were all volunteers for the purpose. They have been kept strictly apart from all trench fever patients while with us, and the first fifty experiments were performed on men who were housed in buildings at some distance from the hospital.

Every man was observed for some days before any experiment was performed on him. In addition to the ordinary physical examinations, with pulse and temperature records, polygraph tracings were made, also thorough

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laboratory examinations of blood, stools, urine, and sputum, for the purpose of excluding all forms of dysentery and enteric, undulant fever, tubercle, and malaria.

These men all volunteered from patriotic motives, and are deserving of the highest praise in consequence. We owe a deep debt of gratitude to them and to Dr. Wiggins of Greenwich, who brought us into touch with them.

The expenses connected with this experimental work have been met entirely by the Lister Institute of Preventive Medicine.

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CHAPTER III

IMMUNITY

MANY cases reaching us from France gave a history of repeated attacks of trench fever. Were such attacks reinfections or relapses ?

We have attempted to reinfect twenty-one men by means of intravenous inoculations of citrated trench fever blood from acute cases of the disease, or by infective louse excreta rubbed into the scarified skin or injected in emulsion subcutaneously, with the following results :

Nine of the twenty-one men were reinfected or caused to relapse. Of these nine men three were free from signs of trench fever when experimented on, the other six all showed evidence of a persistent infection, and in them superinfection may be supposed to have taken place. Twelve men (nineteen tests) did not appear to be affected by inoculations of virulent blood or louse excreta. Of these twelve men six were free from signs of trench fever when inoculated and six were not.

It will be seen that 52 days was the shortest time from the commencement of the original trench fever that any man proved susceptible to superinfection. On the other hand, in Experiment 105, Reynolds proved to be immune to a very large dose of louse excreta as late as 182 days from the beginning of his first attack. In this experiment 20 milligrams of louse excreta, proved to be infective by Experiment 99, were applied to the scarified skin. Five other men proved to be immune

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TABLE III.—Immunity Tests by Inoculation of Trench Fever Blood

Column 3 gives the source of original infection:
N = Natural infection.
E = Infection by louse Excreta experimentally.
B = Infection by trench fever Blood inoculation.

Experiment Number.	Name.	Source of Original Infection.	Day of Disease when tested.	Symptoms of Trench Fever on Day of Test.	Result.	Day of Disease of Patient from whom Blood was obtained.	Amount.	Remarks.
35	Carter	N.	62	Headaches and leg pains	–	63	5 c.c.	
37	Mead	N.	99	D.A.H. and debility	–	2	5 c.c.	
49	Carter	N.	98	Pain in legs	–	2	5 c.c.	
65	Tyler	N.	119	Fit	–	7	4 c.c.	
89	Reynolds	E.	119	Fit	–	1	20 c.c.	½ c.c. of same blood produced infection in a healthy man.
103	Libby	B.	48	Fit	–	7	20 c.c.	
108	Bass	N.	80	Pains in head and legs	–	4	20 c.c.	
110	Du Faur	N.	85	Pains, head, and fever (99°)	–	8	20 c.c.	
111	Pecksen	N.	70	Pains, head; spleen +	+	8	20 c.c.	
112	Kirkland	N.	65	D.A.H., pains, head and legs	+	8	20 c.c.	
115	Carpenter	E.	122	Fit	–	2	50 c.c.	
116	Evans	E.	116	Fit	–	2	50 c.c.	
125	O'Connor	E.	139	Fit	–	1	50 c.c.	

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TABLE IV.—Immunity Tests by Inoculation of Excreta from Trench Fever Infected Lice

Column 3 gives the source of original infection:
N = Natural infection.
E = Infection by louse Excreta experimentally.
B = Infection by trench fever Blood inoculation.

Experiment Number.	Name.	Source of Original Infection.	Day of Disease when tested.	Symptoms of Trench Fever on Day of Test.	Result.	Amount.	Remarks.
20	Dawson	N.	102	Bradycardia	+		
28	Tullett	E.	30	Pains	−		
29	Glover	E.	31	Palpable spleen.	−		
51	Wilson	N.	115	D.A.H. and debility	+		
52	Lancaster	N.	117	Dyspnœa and pains	+		
70	Robinson	B.	139	Fit	+		
76	Carter	N.	134	Giddiness and pains	−		Infectivity of excreta doubtful.
85	Beswick	N.	48	Headaches, pains in legs	−		Lice fed on himself.
86	Lloyd, O.	N.	52	Pain in back and legs	+		
90	Tyler	N.	149	Slight fever, dizziness, and insomnia	−		Lice fed on himself.
98	Reynolds	E.	154	Fit	−		Excreta 154 days old.
99	Jordan	B.	132	Fit	+		Very resistent to original blood infection.
104	Carter	N.	198	Fit	+	8 mgm.	By subcut. injection.
105	Reynolds	E.	182	Fit	−	20 mgm.	Do.
114	Libby	B.	76	Fit	−	4 mgm.	Do.

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after periods of over one hundred days from their original infections.

Twelve of the men whose immunity was tested were infected originally in France under natural conditions ; seven of them were reinfected or caused to relapse.

Six men had been originally infected by us with louse excreta, none became reinfected or showed any change after reinoculation with louse excreta or injection of large quantities of blood—up to 50 c.c. whole blood intravenously. Four of these six were entirely free of symptoms when tested and two, though afebrile, were still unwell. The four fit men had all been infected more than one hundred days previously.

Three men had been originally infected by blood injections, two of them became reinfected, though free of all signs of trench fever when experimented on.

Of the twelve patients whose immunity was tested by intravenous injection of whole blood from trench fever patients two only showed evidence of superinfection.

CHART 33

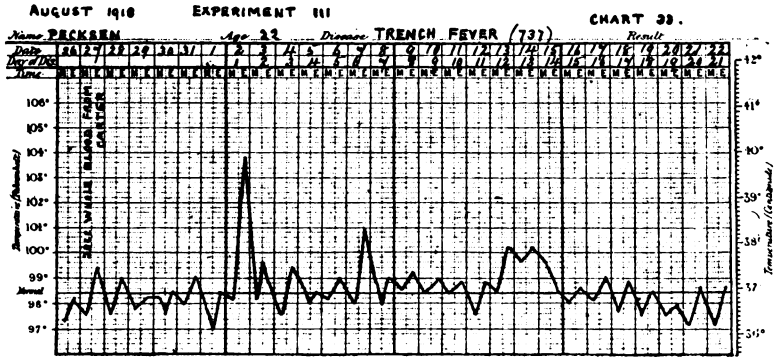

CHART 33.—The result of reinfection with 20 c.c. whole blood intravenously on 70th day of illness. Original infection under natural circumstances in France. The patient was making good progress when reinfected.

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It will be seen that the first of the two was but slightly febrile when tested on the 70th day of his disease, at which time he was making a steady recovery. Six days after inoculation he had a definite relapse of trench fever, followed by rapid improvement and later two further relapses. His spleen, which was palpable when the test was made, did not enlarge further nor become tender during the relapses.

CHART 34

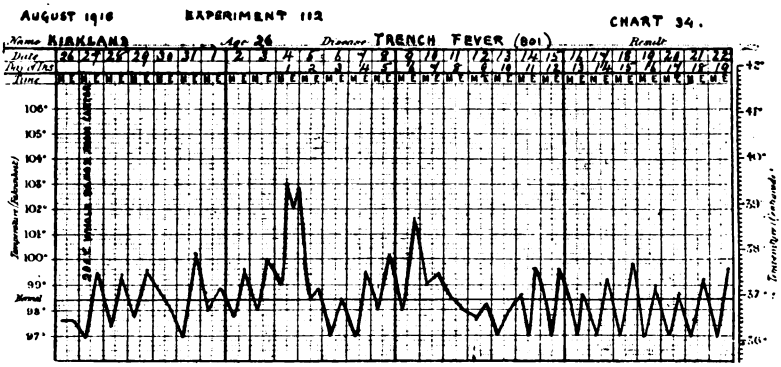

CHART 34.—The result of reinfection with 20 c.c. whole blood intravenously on 65th day of illness. Original infection under natural circumstances in France. The patient was making no progress when reinfected. Charts 33 and 34 should be compared from this standpoint.

The second of these two patients had only reached the 65th day of disease when tested. At this time he complained of pains in the limbs, body, and head, and was constantly slightly febrile in the evenings. He suffered from D.A.H., but his spleen was neither tender nor palpable. He did not appear to be improving, and was obviously unwell. An hour and a half after the blood injection he complained of great pain all over the body, severe frontal and bitemporal headache, and went to bed. He passed a bad night, owing to pain, but his temperature did not rise higher than usual.

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Two days later he appeared in his usual health, and remained so till the 9th day, when a sudden and acute relapse occurred. The spleen became palpable, the extremities cyanosed and rose spots and fine petechiæ appeared on the trunk. Pains were severe and chiefly muscular. A further relapse and much irregular fever followed. During two and a half months that we kept this patient under observation he lost eighteen pounds in weight.

It is obvious that he had developed practically no immunity to his trench fever infection on the date he was tested—the 65th day of his disease.

It will be observed that the amount of blood used for inoculation in these tests was steadily increased throughout the series, and that not until it had reached 20 c.c. was any relapse or reinfection induced. In Experiment 89, 20 c.c. of whole blood from an active case of trench fever on the first day of disease failed to reinfect a healthy man, whereas 0·5 c.c. of the same blood, obtained and injected at the same time, gave rise to an acute and typical attack of trench fever in an uninfected man (Experiment 87).

It would appear, therefore, that in this man's case a considerable degree of immunity had followed his original experimental infection with louse excreta 119 days previously.

Three other fit men, on the 116th, 122nd, and 139th days from their original experimental infections with louse excreta, proved to be immune to the injection intravenously of 50 c.c. of whole trench fever blood into each, the blood being obtained from very active cases on the first and second days of disease.

This resistance to reinfection with whole blood is somewhat striking when it is remembered with what constancy 5 c.c. or less of such blood will infect a man who has never had trench fever.

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Of the thirteen patients whose immunity was tested by the inoculation of excreta from trench fever infected lice, seven relapsed or were reinfected as a result. Of these seven three only were fit men, and they had reached the 132nd, 139th, and 198th days respectively from the onset of their original attacks. The charts of these reinfections (35, 36, 37, 38, and 39) seem to indicate that when a fairly fit man, whose resistance may be supposed to have been raised, is reinfected in this way he tends to react quickly to the reinfection, and so to produce a spiky or Type C or F temperature curve.

In connection with these tests for immunity may be described two Experiments (7 and 19) performed on a volunteer named Jordan. This man came to us on February 2, 1918, and careful examination revealed him to be thoroughly fit.

CHART 35

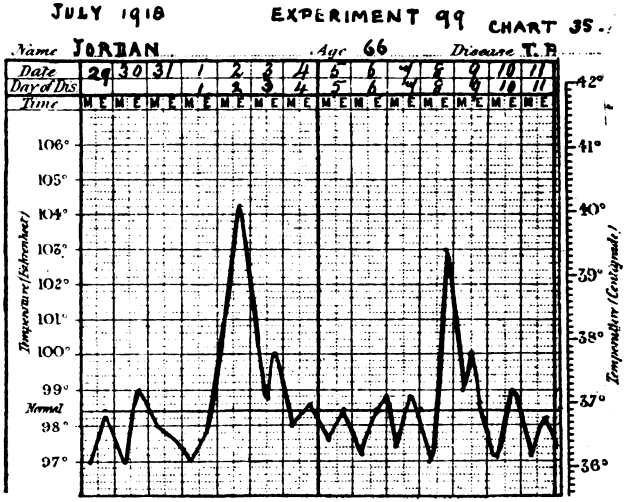

CHART 35.—Reinfected with louse excreta on 132nd day from onset of original attack. Primary infection by intramuscular injection of whole blood.

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CHART 36

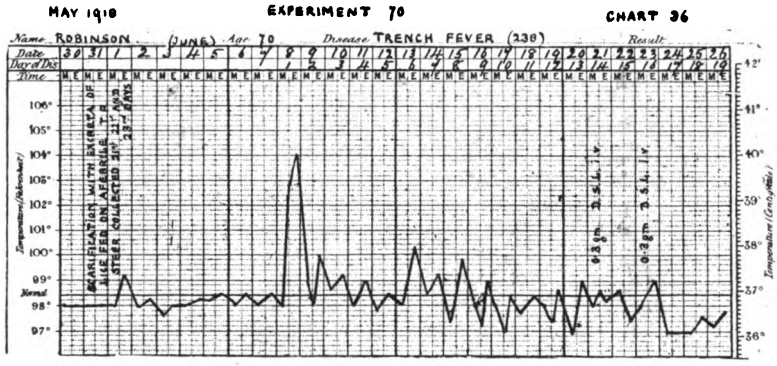

CHART 36.—Reinfected with louse excreta on 139th day from onset of original attack. Primary infection by intravenous injection of whole blood.

CHART 37

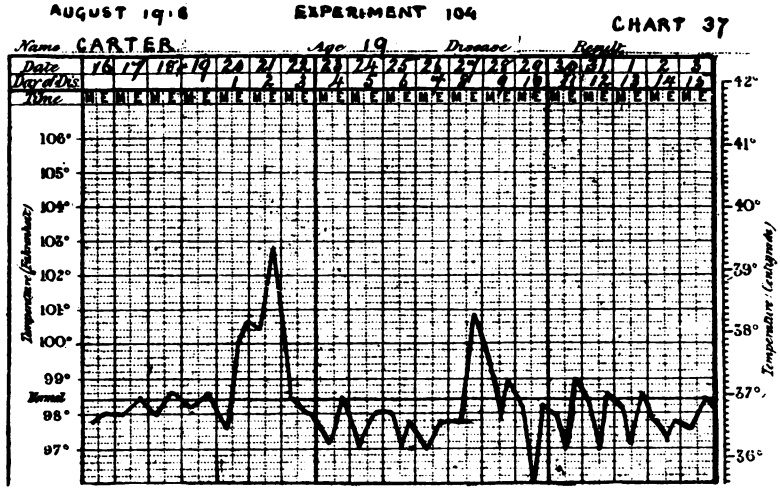

CHART 37.—Reinfected with louse excreta on 198th day from onset of original attack. Primary infection acquired naturally in France.

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CHART 38

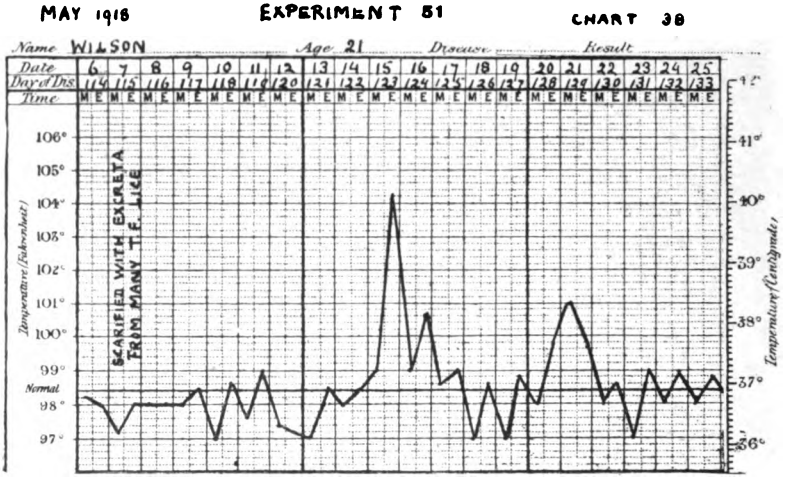

CHART 38.—Reinfected with louse excreta on 115th day from onset of original attack. Primary infection acquired naturally in France.

CHART 39

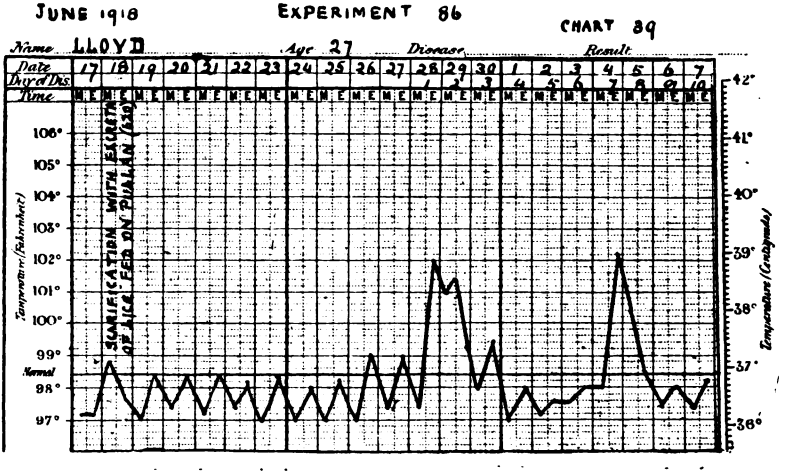

CHART 39.—Reinfected with louse excreta on 52nd day from onset of original attack. Primary infection acquired naturally in France.

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He gave a history of small-pox in youth and of having been lousy each year while hop-picking, but no history of any illness suggestive of trench fever.

On February 4th, 5 c.c. of venous blood were withdrawn from the volunteer infected by intravenous blood inoculation in Experiment 3, whose temperature at the time was 100·4°, this day being the third of his initial attack. The blood was drawn up into a syringe containing 3 c.c. of a 1·8 per cent. solution of sod. cit.; half a minute later the total fluid contained in the syringe was injected deeply into the muscles of Jordan's right buttock. For thirty-eight days after this Jordan remained in good health. Before this experiment could be accepted as evidence that trench fever cannot be passed through two successive men by means of the syringe alone, it was necessary to infect Jordan in some other way. Experiment 19 was therefore performed. On March 13th, 5 c.c. of venous blood were obtained from an active case of trench fever—the syringe into which it was drawn containing 1 c.c. of 1·8 per cent. sod. cit. solution, and the whole injected deeply into the right buttock of Jordan as before. The patient from whom the blood was obtained had contracted his disease in France, and had reached the 51st day of his illness. His temperature was 101·6 at the time, and he was complaining of aching pains in the back and legs, with painful shins. His spleen was both palpable and tender, and his skin was acting freely. He has since had acute febrile relapses on the 58th and 67th days of his disease.

Eight days after receiving the injection Jordan complained of slight tingling sensations in the back. The following day he was feeling generally unwell, and his right thigh ached while out walking before breakfast. That night he slept badly owing to aching in both thighs. There was no shivering or frequency of micturition. In the morning

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he complained of feeling hot at intervals, and at 11 A.M. was noted to be sweating slightly. At this time two-hourly observations of his temperature were being made, and no fever could be detected. He complained, however, of dull frontal and occipital headache, with impaired vision, pain in both arms from shoulders to finger-tips, and pain in both thighs from hips to knees. The thigh and gluteal muscles were tender on pressure, and the skin over these areas was exquisitely tender to touch. There was, however, no evidence of local inflammation at the site of injection. There was no backache at this time, and no tenderness or enlargement of liver or spleen. All the joints were normal and the tongue clean. By the next day there was a great decrease of all symptoms. On the 15th day after the injection Jordan was up and in his usual good health.

On the 19th day he took to his bed again, with frontal headache, pink eye, pain and tenderness in the lumbar muscles, and slight muscle pain and tenderness in both thighs. Tenderness was well marked in the splenic area, but the spleen could not be felt. After forty-eight hours Jordan was quite fit again, and remained so. **At no time throughout his illness was he detected to have a raised temperature.**

This attack so strongly suggests trench fever that we are inclined to believe that it is an afebrile form of the disease. Lice were fed on Jordan while his symptoms were acute, and excreta from them have produced a febrile illness in another man (Experiment 56), thus confirming the nature of Jordan's illness. Jordan proved himself to be refractory to infection, and might at one time have been thought to be naturally immune.

That a naturally immune man may sometimes be met with is possible, but that the percentage of such individuals is small, among cleanly peoples, is certain. Of fifty-three

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healthy men inoculated by us with supposed infective material, its infectivity not having been destroyed by disinfectants, heat, or other means, no less than forty-nine have contracted trench fever.

Of the four men who did not contract trench fever two were inoculated with portions of the same sample of louse excreta. These excreta were not known to be infective, but as the lice from which they were collected had passed excreta on the previous day which caused infections experimentally, and as they passed excreta subsequently which were proved to be infective, they may be supposed to have been infective also. That two naturally immune men were selected by chance for inoculation with one sample of infective excreta, and so failed to react, is however less likely than that the excreta were not actually capable of producing infection. Unfortunately neither of these men remained with us for further tests.

The third man (Experiments 100 and 107) was, on two separate occasions, inoculated with the guts and gut contents of two single lice. The excreta from these lice had not been proved to be infective, but the lice had fed for many days on trench fever patients, who had certainly infected other lice, and may therefore have been infective, as we know the percentage of lice becoming infected eventually, while so feeding, is high. No further attempts have as yet been made to infect this man. None of these three men therefore can be accepted as naturally immune with any degree of certainty. If they are excluded we see, before we turn to the consideration of our fourth exception, that in England the naturally immune man is extremely rare.

The fourth man, named Chilvers, has received four inoculations with louse excreta, of proved infectivity, as follows:

Experiment 94.—The excreta were heated to 100° C.,

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dry heat, for twenty minutes and subsequently applied to a scarified skin area on Chilvers' arm. No signs of trench fever resulted during the next twenty-six days, and this degree of heat was considered to have sterilised the excreta.

Experiment 102.—An emulsion in normal saline was made of louse excreta which had been carefully weighed. Subcutaneous injections of this were given to three men (Experiments 96, 97, and 102) as already described, the first man receiving an amount equivalent to 2·0 milligrams of louse excreta, the second 0·1 milligram, and Chilvers 0·05 milligram. The first two men contracted trench fever, whereas Chilvers remained healthy for twenty-five days after the injection.

Experiment 109.—This last experiment was at once followed by the injection of a fresh emulsion in normal saline made from a further portion of the same sample of louse excreta. This sample of excreta had been thoroughly dried, ground fine in a mechanical grinder, and mixed before being used for this series of experiments. Two hours after the emulsion was prepared an amount equal to 0·1 milligram of excreta was injected subcutaneously into Chilvers. During twenty-seven days' further observation Chilvers remained healthy, though he had received the same size dose, of the same sample of louse excreta, as had produced infection in Experiment 97. At once a third injection was given.

Experiment 130.—The same sample of louse excreta was employed, it being now only seventy days old, and an emulsion made as before. The equivalent of 2·0 milligrams of excreta was injected subcutaneously immediately after emulsification was complete. Chilvers remained fit for twenty-five days while under observation, and this after an injection of a definitely infective dose of a definitely infective excreta (as proved by Experiment 96).

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Is Chilvers a naturally immune man, or has an artificial immunity been induced in him by a series of inoculations with infective louse excreta, the first injection (Experiment 102) being a subminimal infecting dose ? The latter supposition seems a possibility which we are now following up.

In any case we must accept as facts that

(1) **The percentage of men in England naturally immune to trench fever is extremely small.**

(2) **A certain degree of immunity follows an attack of trench fever,** more particularly when it has resulted in a complete clinical recovery. And that **this immunity may persist for six months or longer** (Experiment 105).

(3) **Some cases of ' trench fever ' are afebrile throughout.**

It will be seen in the table of immunity tests (p. 66) for which louse excreta were employed that two attempts (Experiments 85 and 90) were made to reinfect with the excreta from lice fed upon the patient himself. This was done to ascertain whether a man who remained lousy after the onset of trench fever was capable of reinfecting himself from the lice upon him, and so perhaps producing the more chronic and obstinate forms of the disease. In both cases the excreta were collected from the lice and inoculated into the patient during the lifetime of the lice. The first man had been ill for 48 days when the inoculation was made, and though the excreta were proved to be infective (Experiments 99 and 104) no signs of reinfection followed.

The second man had been ill for 149 days when experimented on, and was slightly febrile and far from well at the time. No evidence was obtained that his condition was in any way influenced by the inoculation he received.

It would appear, therefore, that **persistent lousiness is not the usual cause of the more chronic cases of trench fever.**

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CHAPTER IV

PATHOLOGY

THE evidence at present available shows that the organism of trench fever exists in the circulating blood from the first day of the attack till quite late in the disease. We ourselves have produced infections from cases on the 51st, 79th, and 300th days of disease, so proving the prolonged period of infectivity. During this time the blood is infective for lice both while the patient is febrile and afebrile, though there is evidence that the infectivity of the blood diminishes as the disease progresses.

McNee, Brunt, and Renshaw (*Brit. Med. Jour.*, 1916, i. 225) proved that the whole blood is infective when injected intravenously, and we have found (Experiment 87) that 0·5 c.c. of such blood from an early acute case is a sufficient quantity to produce trench fever when so injected. McNee showed further that the serum alone did not cause infection, and we have confirmed this observation on one occasion. His conclusion, however, that the virus of trench fever is intracorpuscular in situation has more recently been disproved by Strong and his fellow-workers in France. The evidence adduced by the latter would seem to show that the virus is free in the plasma, though frequently the corpuscles are only freed with difficulty therefrom by washing.

The causative organism itself remains to be demonstrated, as cultural and staining methods have, so far, failed to reveal it in the blood. Fluid obtained by puncture of the spine,

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liver, and spleen, also bone and bone marrow, have given equally negative results.

Strong is of opinion, from the results of his work with emulsions of louse excreta and urine, that the virus is filterable and ultramicroscopic during at least some period of its existence. The filters he used, however, were apparently tested with *B. typhosus* only.

Our own experiments have shown that the virus, as it exists in the blood, is destroyed by mixing the blood with large quantities of distilled water.

An emulsion of excreta in normal saline we have found to retain its infectivity for twenty-four hours, though infection only resulted after eighteen days' incubation (Experiment 141).

We have submitted samples of the louse excreta with which we have experimented to Arkwright and Bacot at the Lister Institute, and their findings may best be given by quoting from their paper, written with Martin Duncan (*Brit. Med. Jour.*, Sept. 21, 1918):

'Töpfer, da Rocha-Lima, and a few other workers have shown that lice caught on trench fever patients contain large numbers of rickettsia bodies, and that if lice believed to be free from infection are fed on a patient, rickettsia bodies appear in their guts after about five to eight days from the first infecting feed, provided that the lice are kept at a temperature of 30° to 32° C. between the feeds.'

Rickettsia bodies resemble diplococci or bipolar bacilli of very small size—0·3 by 0·3 to 1·5 microns—are non-motile and are best demonstrated by staining for sixteen to twenty hours with weak Giemsa stain (1 drop per c.cm.). Attempts to grow the parasite on artificial media have usually failed, though some successful cultures have been reported.

Such bodies were first described by Ricketts (*Journ.*

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Amer. Med. Assoc., January 30, 1909) as occurring in the blood of patients and in the insect vector of Rocky Mountain spotted fever. Later they were described by Ricketts and Wilder (*Journ. Amer. Med. Assoc.*, April 23, 1910) in typhus fever under similar conditions.

'The following observations have been made, confirming and extending those of previous workers :

'1. If a box of lice is fed on a trench fever patient, and the excreta collected after a period of about ten days, large numbers of rickettsia bodies can almost invariably be found in films. Smears of the guts of lice from such a box contain large numbers of these bodies after about the same interval of time. Of 253 specimens, from boxes of lice which had been fed on trench fever patients at least five days previously, 150 showed rickettsia bodies, 83 gave a negative result, and 20 a doubtful result.

'2. The excreta from sixteen boxes of lice which were examined daily after an infecting meal showed rickettsia bodies for the first time twice on the fifth day, three times on the seventh, three times on the eighth, four times on the ninth, three times on the tenth, and once on the twelfth day from the first infecting meal. When first seen, only small numbers were noted in the films, but three or four days later enormous numbers appeared. These experiments show that after an infecting feed there is a period during which these bodies are not recognizable on account of their small numbers, or of some difference in form. When a box has once become infected with rickettsia, the excreta collected from it continue to show the bodies for two or three weeks, or till the lice which partook of the infecting feed are dead.

'3. All lice from an infected box do not show rickettsia ; only a small proportion do so in the first week : the proportion increases until, after two and a half to three weeks,

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the great majority show these forms. Experiments at Hampstead have also made it probable that after the same time a considerable proportion of lice are infective.

'4. Trench fever patients can infect lice with rickettsia bodies during the fever, between the attacks, or even several weeks after an attack during a non-febrile period.

'5. Normal lice, fed on persons who have not been exposed to trench fever infection, have remained free from rickettsia. Of 245 specimens, from twenty-two boxes fed on seven healthy persons, only one specimen of excreta was found to contain forms which closely resembled rickettsia microscopically. It is not surprising, considering the difficulty in recognizing such small bodies by their morphology, that occasional errors should occur. Four other specimens from two boxes showed these bodies, but they were being fed on a man who had been working with infected excreta in the laboratory for five weeks, and had also been feeding infected lice on himself for the same period. He developed trench fever three days after the first of the four positive specimens was found. It is most probable, therefore, that he had been infected for some days before the bodies were observed in the lice.'

'The Similarity of the Properties possessed by Trench Fever Virus and Rickettsia Bodies, and Coincidences in their Occurrence in Lice.

'1. Rickettsia bodies are very small, often about 0·3 by 0·3 micron in size, and approach the limits of filterability by a Berkefeld filter. There is also some difference of opinion as to whether trench fever virus and typhus virus can pass through a Berkefeld filter.

'2. Rickettsia bodies can to a great extent be separated from larger bacteria in an emulsion of excreta in salt solution by differential centrifugalization. The Medical Investiga-

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tion Committee in France states that blood plasma centrifuged free from cells still contains the virus of trench fever.

'3. Lice do not, according to two series of inoculation experiments carried out by Major Byam, become infective (as shown by inoculation of their excreta) after an infecting meal, for five to ten or twelve days, and rickettsia bodies do not make their appearance till about the fifth to the twelfth day.

'4. All the lice in an infected box are not infective, nor do all contain rickettsia during the second week after the first infecting feed. In one experiment carried out at Hampstead, two lice, one showing and the other not showing rickettsia, were selected from a box on the eleventh day from the infecting feed, and they were inoculated separately into two different men. The louse with rickettsia caused trench fever and the other did not.

'5. In fifty-three experimental inoculations of volunteers at the New End Hospital, the lice or excreta of lice, used as virus, were also examined microscopically. In every case the lice had previously been fed on a trench fever patient. Twenty-seven specimens showed rickettsia bodies and caused trench fever.

'Ten specimens did not show rickettsia bodies, and did not cause trench fever.

'One specimen showed rickettsia bodies, but did not cause trench fever.

'Two specimens did not show rickettsia bodies, but caused trench fever.

'Four specimens gave a doubtful result microscopically, or the inoculation was followed by fever of a doubtful nature.

'Nine specimens showed rickettsia bodies, but did not cause trench fever because the virus had been heated or

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treated with disinfectant, or because the volunteer inoculated had recently passed through an attack of trench fever and was probably immune.

'The agreement between the demonstrable presence of the virus and of the rickettsia bodies is very close. If the thirteen cases which gave a doubtful result, or in which agreement was not to be expected on account of disinfection of the virus or immunity of the patient, are excluded, then forty cases remain, and the agreement between the two methods of examination in thirty-seven is complete—that is, 92·5 per cent.

'These facts indicate the striking interdependence of trench fever virus and rickettsia bodies, though the proof of identity is still wanting, and the inability to obtain definite cultures of rickettsia bodies up to the present hinders further advance in this direction.'

'CONCLUSIONS.

'1. The constant presence, after a suitable lapse of time, of rickettsia bodies in lice which have been fed on a trench fever patient has been confirmed.

'2. The absence of rickettsia bodies from lice bred in captivity, and fed only on healthy men, has been shown by our work, in contradistinction to observations made on the Continent, where the population is much more exposed to infection, and a clean stock of lice is more difficult to procure than in this country.

'3. A very close correlation has been shown to exist between the presence of rickettsia bodies in lice or the excreta of lice, and the virulence of these materials when inoculated into men.'

Since this paper was written we have twice, in conjunction with Arkwright, confirmed the observation that lice,

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after feeding on a trench fever patient, show rickettsia bodies in their guts and excreta provided that the lice are kept between feeds in an incubator at a temperature of 27° C.; whereas lice from the same batch, fed on the same patient, at the same time, if kept between feeds at room temperature (17° C.) do not develop rickettsia. On one occasion we were able to inoculate into two volunteers excreta from lice treated in this way (Experiments 117 and 118).

The lice kept in the incubator and those kept at room temperature both proved infective, though the former showed rickettsia bodies in the excreta, and in excreta from the latter none was demonstrated. A similar amount of excreta was used in each experiment, and the clinical attacks produced were identical, with the exception that the patient receiving the excreta containing rickettsia suffered from shin pains and the other did not.

The incubation periods in the two cases were ten and nine days respectively. A box of lice was fed on each of these men during their trench fever attacks, and in both instances rickettsia bodies subsequently appeared in the lice. One louse, from the box fed on the man infected by excreta showing no rickettsia, inoculated into a volunteer (Experiment 143), gave rise to an attack of trench fever after nine days. This louse was demonstrated to contain rickettsia before being used for this experiment.

It is evident, therefore, that **comparatively low temperatures (17° C.) do not prevent the development of the trench fever virus in the louse.**

The following two experiments were conducted to test the possible correlation between the presence of rickettsia in the excreta of lice and the previous feeding of these lice on cases of trench fever. In each experiment from the commencement the individual lice were kept on fragments of

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linen in separate tubes, plugged with wool, the excreta collecting in the bottoms of the tubes. About twenty lice were used in each series, and half were fed on a case of trench fever and half on healthy men who had never suffered from the disease. In the first Series (A) an examination of the excreta of each louse was made the day before the infecting feed. At about the time when previous knowledge told that the excreta would be infective each louse was transferred to a fresh tube on clean linen. The excreta were collected for a few days and then examined for rickettsia. In these examinations the examiner had taken no part in the manipulation of the lice, and was unaware which had been fed on the case of trench fever and which on the healthy men. In each experiment the lice were fed on the forearm twice daily, and between the meals were kept in a thermostat at 30° C. The data of the infections and the results of the examinations are given below.

Series A.

20 lice originating from non-infected stock.

June 7. Preliminary examination.

,, 8. Half the lice fed on Robinson (T. 104°), trench fever case, 1st day of disease. These were subsequently fed on a trench fever patient twice daily.

Remaining half fed twice daily on healthy men.

,, 19. Eleventh day after the infection—the lice were transferred to clean tubes, nine infected and nine non-infected ones remaining alive.

,, 26. Seventeenth day after the infection—the excreta which had been passed since transfer were examined.

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RESULTS OF EXAMINATION

	Trench fever infected lice.		Non-infected lice.	
	Preliminary examination.	Examination after infection.	Preliminary examination.	Second examination.
Number of lice .	10	9	10	9
Excreta examined .	Day before infection	Those passed 11-17 days after infection	Corresponding to those of infected lice	
Rickettsia present in	0	7=78%	0	0
,, doubtfully present in .	0	1=11%	0	1=11%
,, absent in .	10=100%	1=11%	10=100%	8=89%

Series B.—21 lice originating from non-infected stock.

July 25. 11 lice fed on Heyne (T. 101·4°), trench fever case, 6th day of disease. These were subsequently and twice daily fed on old trench fever case. Remaining 10 lice fed twice daily on healthy men.

Aug. 4. Tenth day after the infection—the lice were transferred to clean tubes, all remaining alive.

,, 12. Eighteenth day after the infection—the excreta which had been passed since transfer were examined.

RESULTS OF EXAMINATION

	Trench fever infected lice.	Non-infected lice.
Number of lice . .	11	10
Excreta examined .	That passed 10-18 days after infection	That passed in corresponding period
Rickettsia present in .	10=91 %	0
doubtfully present in	0	0
,, absent in .	1=9 %	10=100 %

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The blood picture in trench fever indicates abnormal activity of the bone-marrow, and a moderate and rapidly varying leucocytosis precedes and accompanies the fever waves. This leucocytosis is first apparent during the latter portion of the incubation period, during which time a steady increase of the total white cells is often observed. Such increase may be first detected as early as four days before clinical symptoms of trench fever become apparent. The count rarely exceeds 30,000 leucocytes per c.mm., and frequently this number diminishes rapidly before or immediately after the onset of symptoms. When the disease is established, the average count ranges between 10,000 and 12,000 white cells per c.mm., and this number decreases but slowly during convalescence.

At times these blood counts will be found useful in differentiating trench fever from infections of the enteric group, in which a leucopenia is the rule. In trench fever the increase of white cells is due to an outpouring of immature polymorphonuclears. In the afebrile intervals the mononuclear elements are relatively increased. This last is probably a condition common to many soldiers at present in the field.

With the fall of temperature the amount of **urine** passed frequently increases, a trace of albumen is often present, and there is a deposit of cellular elements, though evidence of true nephritis is very rare.

See 'Preliminary Report on the Presence of a Filter-passing Virus in Certain Diseases, with especial reference to Trench Fever, Influenza, and Nephritis,' by Major-General Sir John Rose Bradford, A.M.S., Captain E. F. Bashford, R.A.M.C., and Captain T. A. Wilson, R.A.M.C. (*Lancet*, 1.2.19).

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CHAPTER V

DISTRIBUTION OF LOUSE-BORNE DISEASES

SINCE trench fever is conveyed by lice, the possibility must be considered of its being carried to all parts of the world where conditions favour the spread of louse-borne disease. For this reason the distribution of the three diseases, typhus exanthematicus, relapsing fever, and trench fever, which are known to be conveyed by lice, has been shown in a map compiled from the writings of several authorities. (Clemow, *The Geography of Disease*, Camb. Univ. Press, 1903; R. Bruce Low, *The Epidemiology of Typhus Exanthematicus in Recent Years*, 44th Report of the Local Government Board, London, 1914-15; Nuttall, *The Part Played by Pediculus Humanus in the Causation of Disease*, Parasitology, vol. x., No. 1, 1917.)

An attempt has been made by the quality of the shading to show the relative prevalence of typhus and relapsing fever in different parts of the world in recent years. Strict accuracy, however, is not possible because information is scanty from the less civilised parts, and much doubt prevails about the nature of certain epidemics. No account has been taken of the war epidemics, information concerning these being fragmentary. That there have been outbreaks of typhus in Germany and Austria, not only in the prisoners' camps but also among the civil population, is well known. Terrible epidemics have also occurred in Serbia and Roumania, relapsing fever raging at the same time as typhus.

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Typhus Fever.—This disease, once common in Western Europe, is now very rare there, though it still lingers in an endemic form in parts of Ireland and in Brittany, and possibly in S. Portugal. On the other hand, it occurs frequently in Austria, especially in Galicia. In the Balkans before the present war it was not a serious menace, but in Turkey it was often met with at that time. Over the whole of Russia and the mainland of Asia from about 25° N. it is very prevalent, and frequent epidemics are the rule. In Japan and south of 25° N. on the mainland it is less frequent, being apparently absent from the central and southern parts of India, East Indies, and the Malay Peninsula, but reappearing again in the Celebes. From the rest of Australasia it is absent. In Africa it is very prevalent north of the Sahara, and frequent epidemics occur; south of this barrier it has been shown by Mitchell to be endemic in parts of Cape Colony.[1] It has occurred as localised outbreaks in Canada and the United States. The introduction of the disease was generally traceable to Irish immigrants, to whom the outbreaks were often confined. In Mexico it flourishes on the high ground both in endemic and epidemic form, while the same is true of the line of the Andes in S. America. It has been encountered throughout the greater part of S. America, but not recently in Guiana, nor in the West Indies.

Relapsing Fever.—The distribution of this disease in Europe and N. Africa corresponds exactly to that of typhus. In Asia it is less prevalent to the east of the Obi River in the north and the Ural River in the south than to the west of these rivers, though this line has no significance so far as the prevalence of typhus is concerned. The disease has not been definitely reported from Japan, East Indies, the

[1] Mitchell, 'Typhus Fever in the Cape Province,' *Medical Journal of South Africa* (1917), vol. ii., pp. 189-192.

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Malay Peninsula, and Australasia, with the possible exception in Australasia of a single death in W. Australia (Clemow). It has been reported from the greater part of India. Louse-borne relapsing fever has been described as occurring spasmodically over the greater part of N. America; the form occurring in Central and S. America is possibly tick-borne (Nuttall). South of the Sahara in Africa relapsing fever has the tick *Ornithodorus moubata* as vector.

Trench Fever.—So far as we are aware, this disease has been reported only from the war zones and places approximating thereto, including England. It is known to have occurred in Flanders and in France (at any rate from the Vosges to the sea), on the Italian front, at Salonika, in Egypt, and to a small extent in Mesopotamia. It has not been reported from Syria or E. Africa. It has prevailed in Poland, Galicia, and the Bukovina, though whether it has followed the Eastern front to the sea we do not know. Most probably it has. Wells and Perkins, *Journal of Amer. Med. Assoc.*, March 16, 1918, make no mention of it in their detailed account of war diseases in Roumania.

The outbreak of trench fever in Salonika presents some points of interest. The first infections apparently resulted from men recently arrived from France, and numerous others were diagnosed throughout the cold weather. With the arrival of summer, when the men discarded their heavy garments and were in a position to free themselves individually from lice, the trench fever incidence rapidly declined. During the following winter trench fever was practically absent from the force, and has caused no serious amount of illness in Salonika since.

While we are unable, in the present state of our knowledge, to state definitely that lice occur in every inhabited part of the world, it is probable that they do so. They are, however, undoubtedly less plentiful in hot than in cold climates. The

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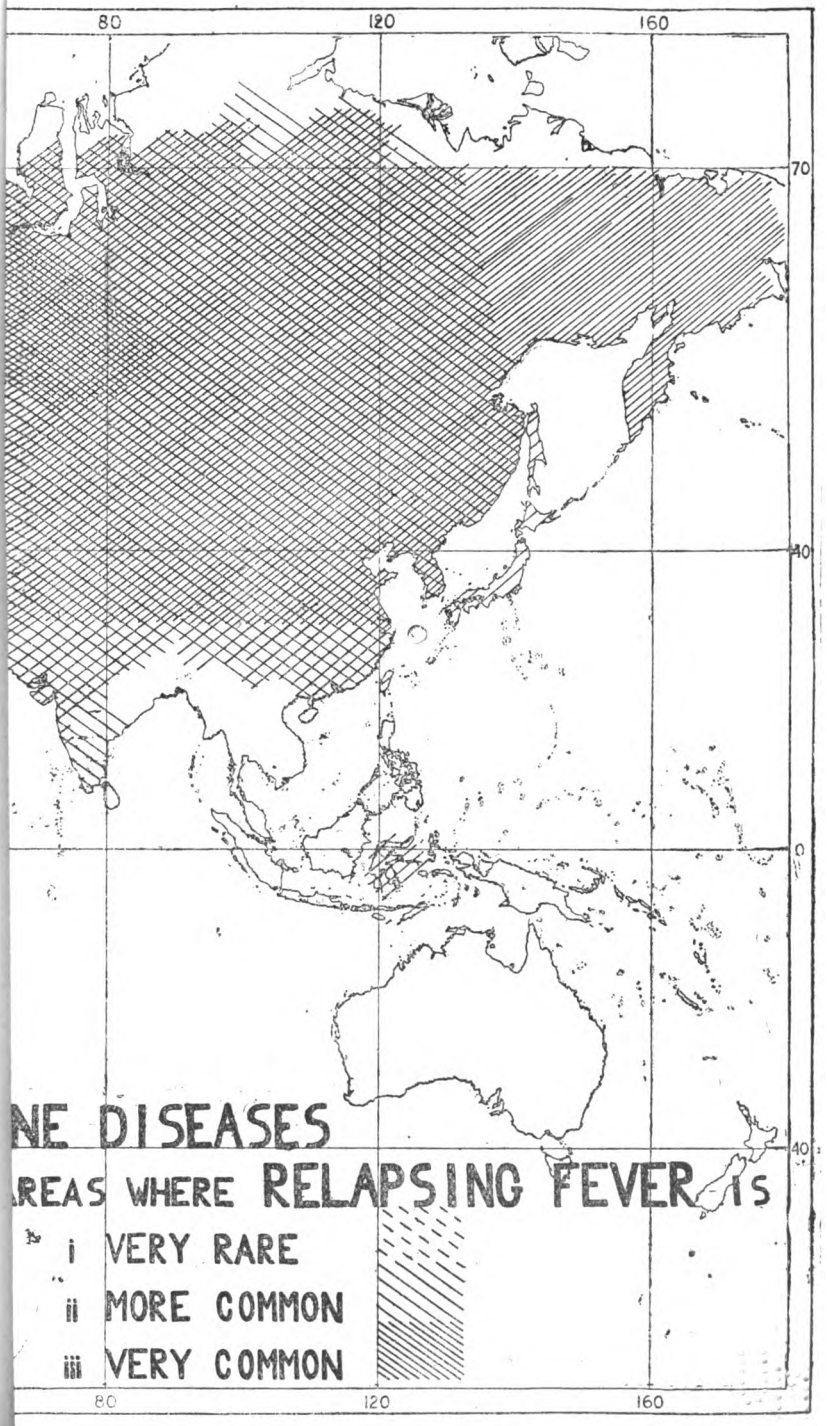

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known distribution of louse-borne disease, therefore, by no means corresponds to the distribution of lice. These diseases are diseases of cold rather than of hot climates, of mountainous rather than of low-lying countries, and prevail in winter rather than in summer. They would appear to have originated in the Old World, and to have been carried to Mexico and Peru by the Spaniards, where they became endemic on the high ground. In Australasia the Tropical Belt appears to have formed a barrier which they have been unable to cross, with the curious anomaly of Celebes. In view of what has occurred in America and the distribution of lice, the introduction of louse-borne disease into any country should be carefully guarded against.

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CHAPTER VI

THE CHRONIC DISEASE

It has become evident that in a large proportion of cases of trench fever invalided to England there is a tendency to advance through a subacute towards a chronic condition, with symptoms of D.A.H. (disordered action of heart), and also in some cases of neurasthenia.

The features of the chronic condition are most easily described by citing the case history of one of our own patients, an A1 man who went through his training without difficulty. In November 1915 he went to France, where he remained at full duty till the spring of 1916, when he 'reported sick' several times with pains in the back, head, and legs. This was diagnosed as 'influenza.' After he returned to duty he noticed much aching in the knee-joints and also some headache. He was admitted to hospital in France three times, each time with fever. In September 1916 he was admitted to hospital (his third admission) with pains in the back and legs, temperature 103·0° F. He was confined to bed for four weeks. A diagnosis of rheumatic fever was made, and the patient invalided to England, where he spent two weeks in bed and ten weeks more in hospital. On getting up he noticed that he was breathless. His headaches continued until his return to France in March 1917. Four days later he reported with fever, and was excused duty for four days. He then finished his retraining. In the middle of June he again reported sick with fever and pains in the head, back, and legs, becoming worse in

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the evening. This time he was excused duty for ten days.

On June 30, 1917, he was sent to a field ambulance with symptoms as above. From there he passed to a base hospital, where he remained fourteen days. He was diagnosed as trench fever and invalided to England. He was admitted to hospital at Hampstead on July 14, 1917. This was approximately the 470th day of the disease. From this date there were frequent small rises of temperature. The patient was a man of good physique, but looking ill. He complained of constant aches in the legs and shins, and said his legs felt like giving way under him. Hands and feet sweating and tremulous. A vivid red tache was present on light stroking. The area of splenic dulness was enlarged to percussion, but on account of tenderness of the left hypochondrium the spleen could not be palpated. The patient complained also of breathlessness on exertion, palpitation of the heart, pain over the precordium, and giddiness, the symptoms known as effort syndrome, or D.A.H. The heart was not enlarged and the sounds were normal. He was markedly exhausted.

This case is not an exaggerated picture of the established chronic trench fever, which may therefore be defined as a state of marked debility, with or without attacks of slight fever and aching, and characterised by a hyperexcitability of the nervous system in general. The symptoms met with may be summarised as follows in the order of their importance: 1, Exhaustion; 2, Giddiness and fainting; 3, Headache; 4, Breathlessness on exertion; 5, Pain; 6, Irritability; 7, Lassitude; 8, Sweating; 9, Coldness of the extremities; 10, Palpitation and cardiac irregularity; 11, Fever.

Before the symptoms are discussed in detail, it must be pointed out that the majority of chronic cases present all the above symptoms.

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In the handling and distribution of cases necessitated by military exigencies, patients with predominant heart symptoms will tend to be evacuated to cardiac hospitals, cases in which nervous symptoms are marked to neurological hospitals, and cases complaining of pains and aches to institutions for the treatment of rheumatic conditions. All these patients, however, if carefully examined, will be found to show, in greater or less degree, the syndrome detailed above.

While it is extremely difficult to prove upon what part of the central nervous system trench fever acts, we believe that a body of evidence exists which points to a specific action on the vagus. This evidence may be grouped under three heads.

Firstly, it was observed by Lewis, while studying D.A.H., that there was a tendency in some of these cases to what was described as ' vagus lag,' *i.e.* a failure of the pulse rate to return to normal after the performance of a specific exercise. In other cases of D.A.H. the pulse returned rapidly to normal. A close study of this phenomenon (the return of pulse rate after exercise) in cases of trench fever has shown that the tendency is for a rapid and even exaggerated return to take place. Thus in a series of eight cases selected at random the pulse returned to below its rest rate in half a minute in two instances, to its rest rate in one minute in six instances. In other words, the pulse had reached its normal rate in all, in normal time. These were cases entering the chronic stage of the disease. In the acute stage a relatively slow pulse is the rule, and the return of the pulse rate to normal after effort is invariably exceedingly rapid. ' Vagus lag,' therefore, in these cases is replaced by ' vagus pull.' This becomes more evident when a comparison is made with the return of the pulse in gas-poisoning controls (Fig. 1).

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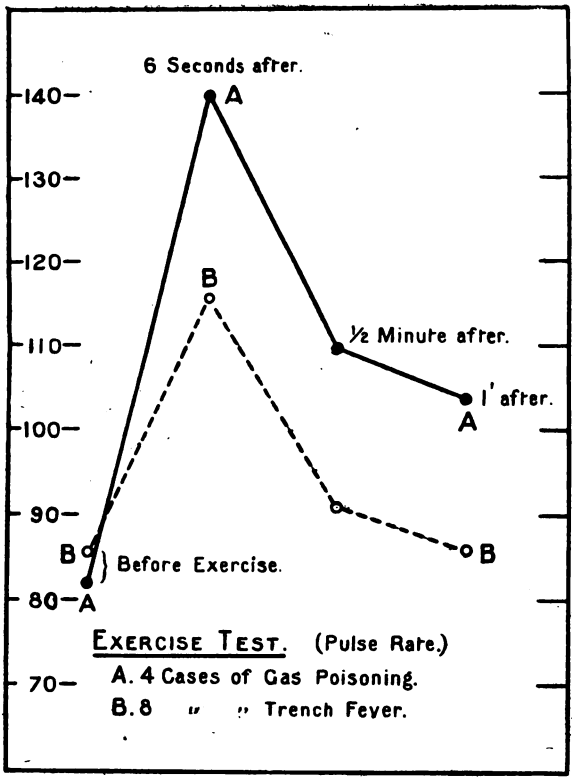

FIG. 1.—Slow return of pulse rate after effort in gas cases. Quick return in trench fever cases.

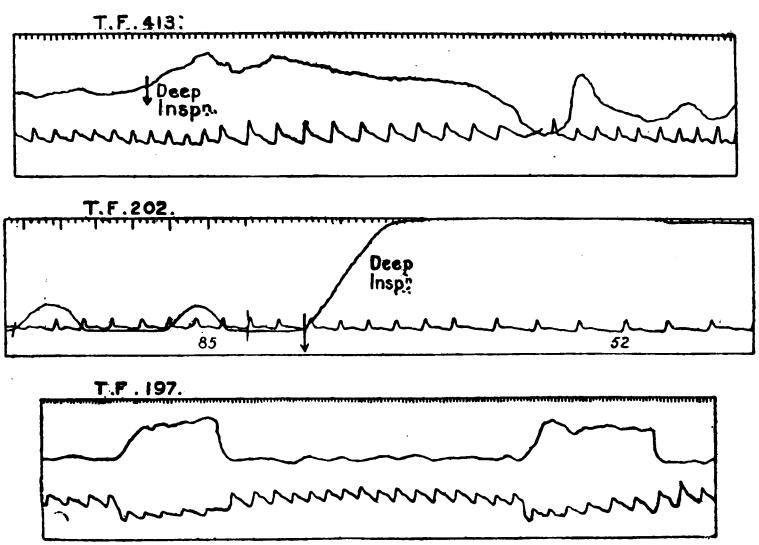

FIG. 2.—Various effects of deep inspiration on pulse rate and volume in cases of trench fever.

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Secondly, it was observed that in a proportion of patients suffering from trench fever a long, deep inspiration was attended by a *marked* slowing of the pulse, with or without loss of volume (Fig. 2). In a few instances loss of volume only was observed. The phenomenon was studied in control cases with no history of trench fever and no symptoms of D.A.H. It was not met with in these cases. To determine whether this slowing of the pulse bore any relationship to vagus activity a number of cases showing it were given a

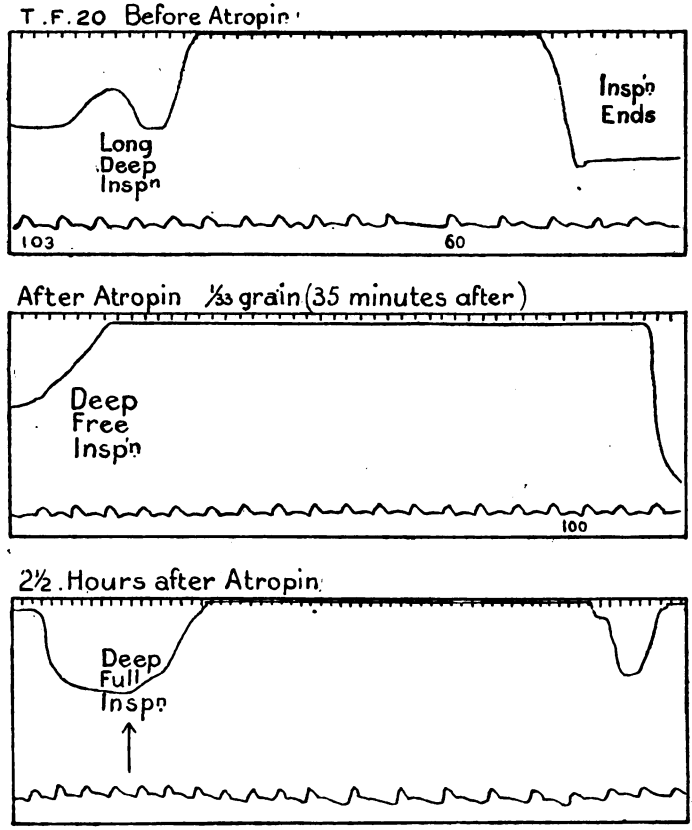

FIG. 3.—Before atropin, pulse slowed markedly on deep inspiration in this case of trench fever. After atropin this phenomenon disappeared, to return when the effect of atropin wore off.

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dose of atropin sulphate (1/33 gr.). In each case atropin was found to abolish, or greatly modify, the effect of prolonged inspiration (Fig. 3). The conclusion, therefore, that the phenomenon was definitely related to vagus activity became a difficult one to refute. (Fig. 4.)

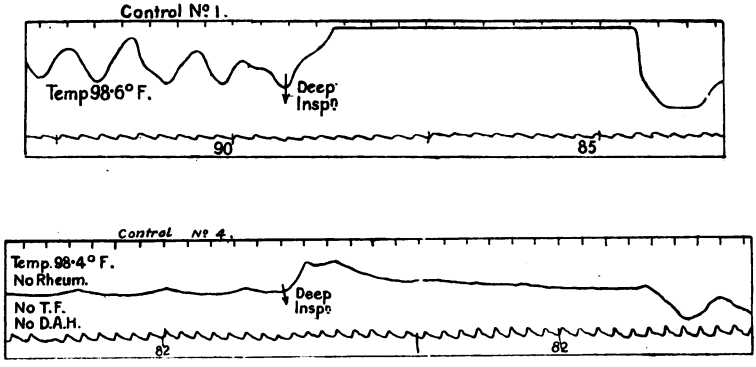

FIG. 4.—Controls: Healthy men. Note absence of slowing or volume fall on deep inspiration.

Thirdly, it was a matter of observation that a number of cases of trench fever revealed cardiac irregularities during exacerbations of the disease, which irregularities disappeared in the intermissions. Chart 40 is of a case which illustrates what we mean. The patient came under our observation suffering from acute trench fever. Subsequently he developed paratyphoid B, as proved by blood examinations, and finally he relapsed twice with characteristic symptoms of trench fever, which symptoms had been conspicuously absent during the paratyphoid attack. During the initial trench fever his pulse tracings showed an extra systole every third beat; throughout the paratyphoid fever no cardiac irregularity could be detected, though the attack was a severe one and the observations made were numerous; while with the trench fever relapses the extra systoles

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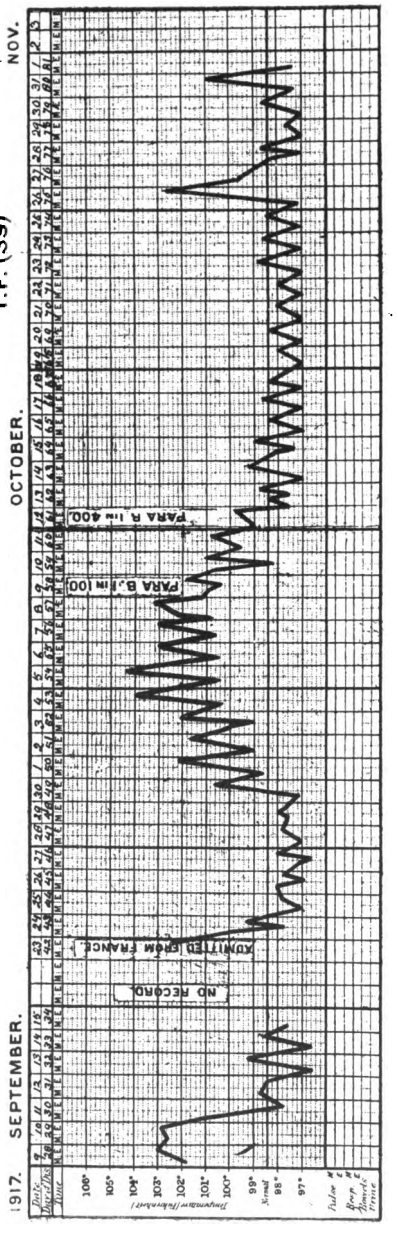

CHART 40.—A case of trench fever in which an attack of paratyphoid B supervened and was followed by two trench fever relapses. Extra systoles occurred during the trench fever attacks, but none was observed during the paratyphoid fever.

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returned as before. Granted that a lowering of the sinus excitability, thus allowing stimuli to arise in other parts of the auricular wall, is a predisposing cause of this irregularity, it is manifest that vagus hyperexcitability would act towards this end.

These three aspects when viewed in conjunction appear to us to offer at least a strong suggestion of a specific action on the vagus in trench fever. This view is strengthened when the tendency to a slow pulse rate in the acute stages, to fainting attacks and collapse, is taken into consideration. Our observations, which are supported by those of the workers in France, show that the transition from bradycardia to tachycardia in trench fever cases usually takes place after the 21st day of the disease, and in the greater number of cases is found from the 21st to the 40th days.

Physical activity is not a necessary factor in the causation of D.A.H., as many cases develop the condition while lying in bed. The impression exists, however, that allowing the patient up does increase the severity of this sequela.

In an attempt to analyse the significance of the change in pulse rate certain coincident clinical phenomena were found to be of importance, *e.g.* profuse sweating, flushing, throbbing of the vessels of the neck, tremulousness, and in some cases discomfort in the throat and chest. These phenomena have been remarked by many observers, and have frequently been ascribed to hyperthyroidism. This view has been disputed, however, notably by Lewis, who found that the administration of thyroid extract by no means tended to exaggerate the symptoms of D.A.H., a state of matters which he suggested might have been expected had hyperthyroidism been the basis of the syndrome. We ourselves, extending Lewis's work, have found in addition that, far

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from exaggerating the symptoms, large doses of thyroid extract distinctly and definitely cause relief.

This finding has been confirmed in so many cases and with such uniformity that the beneficial effect of thyroid is not an accident.

The following are instances of what we mean :

Case 1.—On the forty-sixth day of disease he developed marked sensations of exhaustion, shakiness, profuse sweating, and dyspnœa on exertion. The pulse was rapid, and presented the appearance of D.A.H. on the chart. He was then put on 2 gr. of thyroid extract thrice daily, and immediately the symptoms disappeared. A week later the thyroid was discontinued, and the symptoms returned with a tendency to fainting, severe headache, and giddiness. A further course of thyroid was begun and all symptoms again disappeared. On again being taken off thyroid the symptoms returned.

Case 2.—On the thirtieth day of disease he developed profuse sweating, marked tremor, dizziness, headache, and tachycardia. He was then put on 2 gr. of thyroid extract three times a day, and at once got rid of his symptoms. Treatment in this case has not been discontinued, and the patient remains well.

This experience was met with even in cases which showed definite thyroid enlargement, as the following clearly demonstrates :

Case 3.—In this case thyroid enlargement and discomfort in the neck accompanied the appearance of D.A.H. symptoms. This patient could take 9 gr. of thyroid extract daily without ill effect, indeed with comfort, for he improved steadily while taking it.

It must not be understood, however, that the results of our use of thyroid extract in D.A.H. cases following trench fever have led us to the conclusion formulated by Lewis—

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namely, that hyperthyroidism plays no part in the mechanism of this condition. The most striking feature of the majority of early cases of trench fever is the disinclination of the patient to respond to calls for effort. This disinclination is no local weakness of the legs, but a general extreme exhaustion accompanied by fainting in many cases and by bradycardia. At this point, as has already been suggested, the dilator mechanism is in a high state of excitability and the patient is literally without the power to relieve himself of the depressor effect produced. Indeed, the falling pulse rate and occasional simultaneous gastric disturbances, with sweating and pallor, stamp the attacks unmistakably as vagal and dilator in origin.

After the subsidence of the acute phenomena it is found that the vagus system of these patients is not less excitable than it was at the onset of the disease, but the response to effort has now improved ; in other words, the man is now able, by means of some mechanism which is brought into play, to compensate for the activity of his vagus mechanism when an effort is required of him. A lead in the direction of the true nature of this compensation has been given to us by the fact that, in some cases, enlarged thyroids have been met with, and also by the appearance of phenomena usually associated with hyperthyroidism.

These observations, coupled with the good effects of thyroid administration, have brought us to the conclusion that the so-called hyperthyroidism met with in these cases is in the nature of a compensation to the depressor effects of vagus hyperexcitability.

The work of Cannon, Cattell, and Levy has demonstrated that the mechanism of pressor effects, as opposed to depressor, involves the suprarenals and the thyroid. Cannon and Cattell place the secretory innervation of the thyroid on a firm basis in a work appearing in July 1916 (*Amer.*

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Jour. of Physiology). They show that thyroid secretion resulted from stimulation of the cervical sympathetic nerve and also from adrenal secretion, the latter through the blood stream. That is to say, that at times of adrenal activity a call will be made upon the thyroid secretion.

It is well recognised that vagal stimulation with its resulting depression calls for adrenal or sympathetic activity. This fact is well established in the work of Dr. Roger ('Quelques Recherches Récentes sur les Fonctions des Capsules surrénales,' *Presse Médicale*, November 22, 1917). Roger says: 'When, in a normal rabbit, we excite by a faradic current the peripheral end of the cut vagus we observe a true stoppage of the heart; that is to say, a diastolic fall, sharp and profound, which is almost always followed by a return of the beats. The curve resulting is V-shaped. The first excitation always produces the most marked effect.

'If now we carry out the experiment on a decapsulated rabbit the first tracing obtained looks like the normal tracing, but during the second faradisation the stoppage of the heart is prolonged and the return of the beat is made with difficulty.

'Continuing our excitations we soon obtain diastolic periods lasting as long as 30 or even 40 seconds. . . .

'How are we to explain these differences? We might say generally that the vagus in the normal rabbit shows less and less effect in repeated stimulations because it is becoming exhausted. If this was the correct explanation we should find the same phenomenon in the decapsulated rabbit. But since in the decapsulated rabbit exactly the reverse is found, we are forced to take into consideration the only element that differs in the two series of experiments —the suprarenal capsules. We thus arrive at the following conception.

'When the action of the vagus becomes preponderant,

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when it acts, that is to say, with full force on the heart, a reaction, probably in the nature of a reflex, is produced on the suprarenal capsules which give out adrenalin. This adrenalin counterbalances the action of the vagus, it prevents the stoppage of the heart and raises the arterial pressure.

'This conception leads to the supposition that an injection of adrenalin given to a decapsulated rabbit would cause the heart of that animal to respond like the normal rabbit's heart. That is exactly what happens.'

The work of Cannon and others, already referred to, shows that this reflex stimulation of the suprarenals involves thyroid activity. Consequently the normal reaction of a man to excessive excitability of his vagus system will be a mobilisation of adrenalin and thyroid, and so a reaction based upon the sympathetic system.

Examination of our cases shows that the effect of the toxin is a more general one than a purely cardiac vagal effect. There is in addition to a depressor effect, a circulatory effect, resulting in fainting attacks of definite vagal and depressor origin. In other words, not only is the heart held in inhibition, the wide splanchnic blood lake is dilated and a severe fall of blood pressure, similar to that seen during stimulation of the depressor nerve, results. This effect has been emphasised by Lewis (Report on Soldiers' Heart to Med. Research Com.), as follows, in describing a fainting attack observed in one of his patients :

'The simultaneous fall of pulse rate and blood pressure stamps the attacks as vagal in origin, a view fully confirmed by the occurrence of simultaneous gastric disturbances.'

Adrenalin, as is well known, acts by constricting the splanchnic arterioles and so closing the dilated splanchnic lake. A marked pressor effect results. Indeed, Hoskins has shown that the pressor effect of adrenalin depends

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entirely upon the emptying of this blood lake, since, if the splanchnic area be excluded from the circulation, adrenalin no longer is able to produce any pressor effect.

Levy has conclusively proved that the pressor effect of adrenalin is multiplied from 200 to 300 per cent. if thyroid be present, and he has further proved that thyroid has no effect upon the vagus whatever. Consequently it is evident that, in Levy's words, 'thyroid secretion renders more excitable the sympathetic structures acted on by adrenalin in raising arterial pressure.' It therefore follows that if the blood stream contains an excess of thyroid less adrenalin will be required for any given pressor effect, or, in other words, the accelerator and other effects of adrenalin will be less evident in these cases and effort will be accompanied by a smaller degree of tachycardia. We see in this the explanation of the slowing of the pulse we have met with on thyroid administration.

The Disease in Transition.—We may now proceed to examine more closely the symptoms of the subacute and chronic disease, which symptoms, as we have pointed out, are progressive in character and subject to modification in their progress. Before doing so, however, we would like to insist upon this fact of the modification of symptoms because, unless it is borne in mind, cases will be classified wrongly, and those seen at one period will be regarded as differing from those met with at earlier or later periods; such differences are merely differences of degree. The disease, like most diseases, is a process rather than a fixed point. Each stage presents its own features. Each stage shades into the succeeding stage. When we speak of the chronic disease, D.A.H., neurasthenia, etc., we by no means wish to imply that we believe the evil process is ended or that cure does not take place. The truth is that sufficient time has not yet elapsed to enable us to say whether the

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matter ends there, advances to some further phase of disability, or gradually resolves itself in cure. A proportion of cases certainly appear to establish a *modus vivendi.*

The subacute disease marks the passage from the acute to the chronic disease. The patient at the conclusion of the acute stage is in a condition of lassitude, the result, as we have suggested, of his active vagus. He is content to lie still without doing or thinking, and so remains unaware, in a physical sense, of his condition. During this period the pulse chart and temperature curve tend to be both subnormal. A little later the patient begins to enter once more upon the affairs of life. He is now at once aware of the disability under which he labours—that is to say, of the disturbance in his nervous equilibrium occasioned by his hyperexcitable vagus system. In order to compensate for this the opposing mechanism is called upon to make greater efforts. There succeeds a period of rapid heart action, bouts of palpitation and tendency to sharp relapses into weakness—a period, that is, of unstable nervous balance in which at one time so-called thyroid symptoms manifest themselves, at other times vagal symptoms. Clearly, however, this stage is really a reaching out towards a new equilibrium; that is to say, a balance between the over-excited vagus and the sympathetic mechanism which is becoming over-excited also as a compensation. This new balance is established gradually, the patient, if the analogy may be used, learning to walk or co-ordinate anew. But the new balance differs from the old balance of health in one momentous respect—it is a balance between extremes, the daily swing of rest and activity is therefore greatly exaggerated. Activity becomes restless, nervous, violent; rest becomes heavy, somnolent, deep. The symptoms of so-called D.A.H. are produced and the chronic stage has begun. This passage from the acute to the chronic stage is

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illustrated in the accompanying chart (Chart 41), which it will be seen shows three of the four distinct phases: 1, The acute attack (this is not shown); 2, The period of rest following the attack; 3, The period of badly adjusted nervous balance—rapid pulse, etc.; 4, The period of new adjustment of nervous balance—D.A.H.

Chart 41

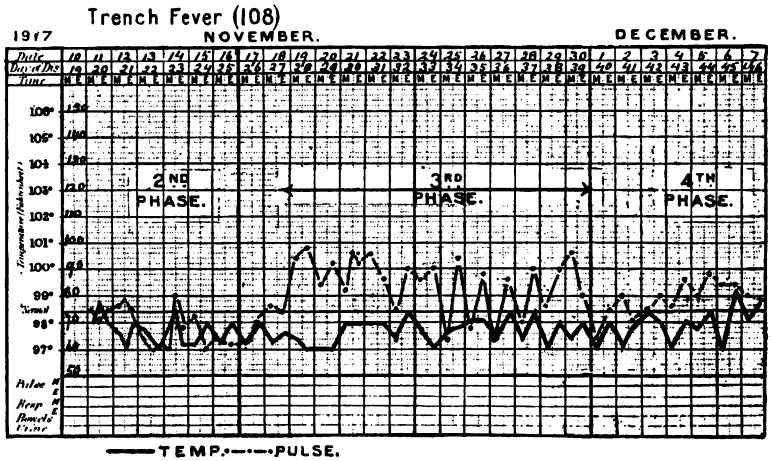

Chart 41.—Showing onset of D.A.H.

It is interesting to recall that in the course of a series of investigations into the nature of D.A.H., Fraser and Wilson found that the response of the patients to adrenalin, the drug of the true sympathetic, was much exaggerated, while the response of the patients to apocodeine, a drug which inhibits the true sympathetic, was also much exaggerated. This finding is in exact agreement with the expectations we might have entertained from our clinical study of the genesis of D.A.H.

The Temperature Curve.—The normal heat of the body depends upon the amount of heat generated and the amount

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lost. There is a daily swing in health showing a low temperature in the early morning and a higher temperature in the late evening. That this swing is determined to some degree by the interrelationship of the pressor and depressor mechanisms is scarcely doubtful. We should therefore expect that when the new equilibrium of our cases was established—what we call the chronic stage or stage of D.A.H.—the daily swing would be of a more exaggerated type in keeping with the exaggerated irritability of the nervous systems concerned in the new balance. This, in point of fact, we find, the daily swing amounting in most instances to 2° F. and often extending considerably above and below the normal limits.

It must be realised, however, that a 'spiky' relapse of fever often occurs during the chronic stage. In these cases nervous balance stands once more in need of a readjustment, the extent of which will depend on the extent of the disturbance produced in the vagal system.

The Clinical Picture in the Transitional or Later Subacute and in the Chronic or D.A.H. Stages.—In the later subacute stage or transitional stage of the disease the patient presents a well-defined clinical picture. Throbbing headache is complained of, the face is flushed, the skin warm, profuse sweating occurs, marked tremor is present, a sense of fulness in the upper chest is complained of. Sometimes constant nausea is felt, and faintness frequently occurs. The patients may faint, and often do so. When the chronic stage or stage of D.A.H. has been established this extreme instability of the nervous system is less well-marked. The patients no longer tend to swing from states of great excitement to states of complete collapse. Another and different clinical picture is met with. This clinical picture corresponds to the entity which has acquired the title of 'neurasthenia,' by some qualified with the words 'of vaso-

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motor type.' No matter what name may be given to it, it will be found that there occur brisk reflexes, coldness and blueness of the extremities, irritability of temper, inability to fix the attention for long periods, exhaustion, usually provoked by sustained effort, far in excess of that evoked by the same effort in healthy men.

Breathlessness on exertion, palpitation, precordial pain and giddiness, are features of both subacute and chronic conditions.

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CHAPTER VII

PROGNOSIS AND TREATMENT

PROGNOSIS

In the acute disease the capacity of the individual to throw off the effects of the infection, and completely regain his previous state of health, is dependent on certain factors which will be considered as follows :

(1) Age.
(2) Past medical history.
(3) Number of attacks.
(4) Early rest after onset.
(5) Individual recuperative capacity.

1. **Age.**—Our experimental infections have shown conclusively that age alone is without influence on the course of the disease. The percentage of rapid recoveries among the old men who make up the bulk of these subjects is quite as high as that of the young men. But age in its reaction to the demands of modern warfare produces a man so diminished in recuperative capacity, that when infected he is less able to throw off the disease than the younger man. This is illustrated by the following comparison. Of 215 replies to inquiries, received from men under the age of 35 who had been discharged from hospital for three and six months, 53, or 25·4 per cent., were still unfit for any form of useful work. Of 53 replies received from men over the age of 35 who had been discharged from hospital for the same length of time, 21, or 40 per cent., were still quite useless.

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2. **Past medical history.**—A bad past history is of the greatest significance. The man, be he young or middle-aged, offers a bad prognosis if his history reveals (*a*) a tendency to infectious diseases, (*b*) a pre-existing disability, recent or remote matters not, so long as his efficiency was appreciably diminished at the time he acquired his infection.

This applies not only to chronic constitutional disturbance, but to local conditions, such as flat feet, sprains of joints in ankle, hip, knee, or spine ; old and recent fractures, and wounds involving bones or joints.

The analysis of a group of 236 chronic cases shows that 43, or 18·2 per cent., were physically unfit when they contracted the disease. Of these forty-three men nine were discharged to duty, while eight had to be discharged from the army as permanently unfit. Six men of this group had febrile relapses after periods of apyrexia which varied from two to five months. The average duration of disability in this group at the time they left hospital was 5·4 months.

3. **Number of attacks.**—This is really included in the last statement, but should receive particular recognition. The man who gives a history of former attacks of trench fever is particularly prone to pass into the chronic stage.

4. **Early rest after onset.**—The earlier the man gets to bed after the onset of the attack, the more likely is he to make an early and complete recovery.

5. **Recuperative capacity of the individual.**—The capacity to sleep, eat, and assimilate are favourable signs ; and, conversely, patients who fail in these offer an unfavourable prognosis.

The condition of the spleen in the acute stage is valueless as a prognostic point. It is frequently enlarged, but not so at any characteristic period, nor is the enlargement persistent. As will be seen below, in the chronic disease, persistence of

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the enlargement is indicative of obstinate and prolonged disability.

The general prospects of complete recovery from the acute disease are good. The experience of physicians serving in France is in close accord with our experimental findings. Both of these records show that of all cases of definite trench fever and P.U.O., about 85 per cent. recover completely and are fit for full duty in about two months. All that follows concerning prognosis in the chronic stage of the disease applies to the small proportion, about 15 per cent., of intractable cases who do not yield to treatment at the Base hospitals in France and are evacuated to England.

The Chronic Stage of the Disease.—The factors first to be considered in arriving at a prognosis in the chronic stage are naturally those which have been shown to influence the course of the disease in the acute stage :

(1) Age, (2) Past medical history, (3) Number of attacks, (4) Early rest after onset, (5) Recuperative capacity of the individual.

In addition, there are those which only become evident after many weeks :

(6) Splenic changes.
(7) Febrile course.
(8) Weight.

The outlook in this stage is always one of prolonged disability, but this will be found to vary greatly in duration as influenced by the factors already mentioned, and now to be considered in detail.

1. **Age.**—Age again appears as an unfavourable element ; the man of over 35, if serving in the field, offering a poor prospect of recovery.

2. **A bad past history** again takes an important place, and affecting as it does all ages concerned should, without doubt, be considered the most important factor.

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3. **Multiple attacks.**—A history such as stated in considering the acute disease is indicative of probable chronicity.

4. **Early rest after onset.**—Evidence that after contracting the disease the man had been, by circumstances, compelled to carry on without rest for some days is a consideration which points very frequently to an obstinate course of the disease. One of the most stubborn and distressing chronic cases we recall is that of Sergeant M. A young man of fine physique, and a good past history, he developed the disease quite suddenly on the night of March 20, 1918; but he stuck it, and served through the retreat on the Somme, only reporting sick about three weeks later when the line was holding firmly.

5. **Recuperative capacity of the individual.**—See prognosis in the acute disease.

6. **Splenic changes.**—A definitely and persistently palpable spleen in this stage is indicative of prolonged disability.

Of the group of 236 cases already referred to, 12 showed a quite definite splenic enlargement which was constant; of these two were discharged to duty, while four had to be invalided from the army. The duration of disability at the time of discharge in this group was 5·8 months. One member of this group had a febrile relapse after five months of apyrexia.

7. **Febrile course.**—The type of fever which may be considered as indicating a prolonged chronic stage is low, irregular pyrexia, which may appear in the second or third week of the disease and which sometimes continues for months.

In the group analysed above 14 cases showed this type of fever. None was discharged to duty; all but two were transferred to convalescent hospitals with symptoms of trench fever persisting; the two exceptions were invalided from the army. The average duration of disability in this

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group on the day of discharge from hospital was 8·9 months. All febrile relapses tend to aggravate the cardio-vascular disturbance known as D.A.H. That this type of fever is particularly prone to do so, and to render the condition permanent, is evident from its persistence and the ease with which it may be overlooked.

TABLE V.—Incidence of D.A.H. in 402 Cases of Trench Fever

D.A.H. due to all causes, 155=38·5 per cent.
D.A.H. due to causes other than T.F., 44=10·9 per cent.
D.A.H. due to T.F. with onset of D.A.H. before admission to Hampstead, 69=17·1 per cent.
D.A.H. due to T.F. with onset of D.A.H. after admission to Hampstead, 42=10·4 per cent.
Average day of disease on which D.A.H. was first recorded in cases developing D.A.H. in Hampstead Hospital, 27·3.
Extremes of onset of D.A.H., 15th—62nd day.

The character and course of the initial attack offers no point of prognostic value. As has been seen above, this is variable, but its variations are without significance. The following table gives an idea of the condition of the whole group as compared to the sub-groups mentioned above.

TABLE VI.—Disposal on Discharge from Hampstead Military Hospital of 236 Cases of Trench Fever

To duty	14	5·9 per cent.
To lower category	12	5·0 ,,
To command depot	22	9·3 ,,
To convalescent hospital	171	72·4 ,,
To civil life as permanently unfit	17	7·2 ,,

Of these, 15, or 6·2 per cent., were free of all symptoms of trench fever on discharge.

Average duration of disability on day of discharge, 4·5 months.

Febrile relapses occur in all types of cases, 8 per cent. of the 236 cases showing a definite febrile relapse with

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temperature of 102° or more after an afebrile period varying from two to five months, during which time the temperature had not exceeded 99·4°.

The percentage of relapses would have been much higher had we accepted the rises to below 102°, which were, as a rule, accompanied by definite subjective symptoms; but in the desire to rule out the subjective element as much as possible, the 102° standard was rigidly adhered to.

The intensity, the seat, or character of the pain, the height of the initial temperature or its duration, the suddenness or otherwise of the onset, give no indication of the future course of the disease.

8. **Weight.**—In the chronic stage a steady gain in weight constitutes the most reliable guide to a favourable prognosis. A constantly declining weight curve is, in our experience, an unfavourable indication.

The following weight chart is that of an obstinate chronic case, and is a true reflection of the constant deterioration

CHART 42

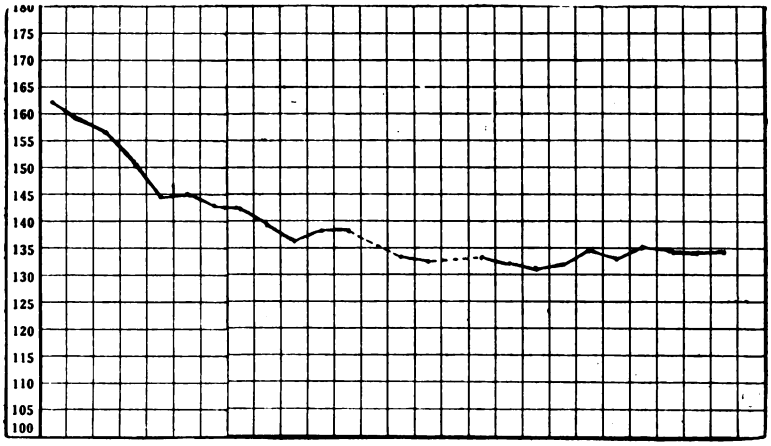

CHART 42.—Weight chart showing weekly observations for a period of twenty-six weeks. A loss of 30¼ lbs. in 19 weeks followed by a gain of 3½ lbs. in 7 weeks.

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of the man during the first nineteen weeks of his stay in hospital. He improved during the next seven weeks, but was eventually invalided from the service.

Progress after discharge from hospital.—In order to keep in touch with our cases and study the continued course of the disease, a 'follow-up' system has been devised.

At the time of discharge from hospital an estimate is made of each patient's condition as to whether it is good, fair, or poor, and this is placed on record.

At the end of three months, and at the end of each succeeding three months, after his discharge, a postcard is sent to him, reply paid, asking him and his medical officer a series of questions. All replies on receipt are considered and marked according to the following standard:

Good.—All men who are quite fit and carrying out as full military duty as they did before contracting trench fever unless prevented by other conditions; and all who have not seen a doctor, reported sick, or entered hospital for trench fever or any of its sequelæ during the period of three months under review.

Poor.—All men who are not doing any useful military work. All who have had a definite attack of trench fever during the previous three months even though now doing full duty. All who have during this period been invalided from the army on account of trench fever or its sequelæ.

Fair.—All those whose condition was intermediate between the two preceding groups.

N.B.—This group includes a number of cases of D.A.H. and myalgia.

From 1st January 1918 to the 16th September of the same year, 415 inquiry postcards had been sent out. 229, or 55 per cent., of the men had replied by the 14th October, one month after the last inquiry was sent out. In this way the number of replies received totals 320 from 229 men.

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Of the 320, 129, or 40 per cent., were fit, and had been for the preceding three months; while 191, or 60 per cent., had shown greater or less evidence of the persistence of the disease during the same periods.

The statement has been made that all but a very small percentage of trench fever patients make a good, complete, and rapid recovery.

While this is true of about 85 per cent. in the acute disease, as has been stated before, it does not in any sense apply to the chronic disease, as is abundantly proved by these figures. Even greater emphasis is given to their value in refuting such an erroneous statement if we assume for the purpose of argument (what is most unlikely) that all of the 186 men who had not replied were quite fit and doing full duty. Even then it will be seen that the average of definitely known disability cannot be reduced to anything less than 37 per cent. of the chronic cases, or considerably more than 5 per cent. of all the infected.

TREATMENT

Specific Treatment.—Clinical signs being the only practical guide available as to the value of any specific treatment, we have controlled our results by means of a large number of unselected cases which were treated by palliative measures only. In this way the conclusion has been reached that no drug or system of therapy which has been tested may be considered as specific.

The published results of other workers and our own clinical experience lead definitely to the conclusion that quinine, the salicylates, and the analgesic and antipyretic coal-tar products are quite useless. In the course of our quest for a specific we have used the following substances in the manner indicated.

Acriflavine.—A 0·1 per cent. solution in normal saline,

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which was given intravenously in doses varying from 10 to 300 c.c. These doses were repeated freely and frequently. Administration by mouth was also tried; 10 c.c. of the solution being given thrice daily; and for as long a period as five weeks in many cases.

Galyl was used intramuscularly in doses of from 0·1 to 0·4 grm., repeated at weekly intervals; intravenously in doses varying from 0·2 to 0·5 grm. These were repeated at varying intervals; in one series three doses of 0·4 grm. were given at intervals of 48 hours.

Collosol Argentum, Iodine, and **Antimony** were used intravenously, all in repeated doses—the silver preparation in doses varying from 2 to 20 c.c., the iodine in doses of from 50 to 300 c.c., and the antimony from 1 to 2 c.c.

Collosol Sulphur, Manganese, and **Palladium** were given intramuscularly in repeated doses—the sulphur in doses of 1 c.c., the manganese 1·5 to 1 c.c., and palladium 0·5 c.c.

Colloidal Rhodium was used intravenously in doses of from 1·4 c.c.

Intramine was used intramuscularly in doses of from 1 to 3 c.c.; this was given in combination with galyl in one series, and with collosol manganese in another.

Kharsivan was used intravenously in repeated doses varying from 0·4 to 0·8 grm.

Eusol (Ritchie's formula) was used intravenously in repeated doses of 100 c.c. each.

Methylene Blue was given by mouth in doses of from 2 to 4 grains (0·12 to 0·25) twice or thrice daily.

Trypan-Red was given intravenously in 10 c.c. doses of a 5 per cent. solution repeated at intervals of 48 hours.

Tartar Emetic.—A 2 per cent. solution was used intravenously in repeated and increasing doses of from 2 to 10 c.c.

Disodo-Luargol was used intravenously, and repeated in increasing doses of from 0·05 to 0·3 grm.

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Foreign Protein, as represented by a vaccine prepared from a 24-hour culture of *B. typhosus* on agar. This was used intravenously, and in each case repeated once after an interval of one week. A small desensitising dose of 500,000 organisms was first given subcutaneously, followed by an intravenous dose of 10 millions in two hours.

'Vaccine Treatment.'—It being quite established that the virus of the disease is in the excreta of the louse, an attempt was made to vaccinate by means of an emulsion of louse excreta sterilised by (*a*) heat or (*b*) phenol. The dose was determined by weight; 2–24 mgm. of excreta being used as a single dose in this series.

The drugs were given in the different series, in varying relation to the fever; before, during, and after the rise.

Treatment of the Acute Disease.—Complete rest in bed is essential. The earlier the patient is put to bed the more likely is a cure to result, or the more favourably is the degree and duration of the disability influenced. This is abundantly confirmed by observation of our experimental infections.

As a prophylactic measure against the development of D.A.H., the patient must be kept in bed until the fever has completely subsided, and should be ordered to bed on the first indication of a relapse.

As soon as the acute illness is over and the man is capable of taking the ordinary ration, even though he be still weak and debilitated, he should be transferred to a convalescent camp, where he must be kept occupied with interesting outdoor exercises, well within the limit of his capacity. He must not be overtaxed or expected to attempt any degree of effort which he cannot accomplish with ease. If such a contingency be not guarded against he is apt to lose confidence in himself, yield to enervating impulses, and pass into the class of so-called neurasthenics.

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Pain and tenderness.—Collosol manganese, in a majority of cases, does modify the pain, and in many gives complete relief in 24 hours; it has no effect on the temperature, and does not prevent a relapse.

Methylene blue ranks next as an analgesic in our experience. Four grains (0·25) or more, daily, may cause painful and burning micturition, and in some cases leads to retention of urine.

Aspirin in combination with phenacetin relieves pain, but is less reliable. Antipyrin is of about equal value.

As a local application a mixture of menthol, 1 drachm (4·0) to the ounce (30·0) of methyl salicylate, applied as a compress under gutta-percha tissue, is, speaking generally, the most satisfactory.

Saturated solutions of Epsom salts and of carbonate of soda applied hot and kept on as a warm compress, are often efficacious.

Sleeplessness.—This may be due to pain, or may be a true insomnia of nervous origin. No matter what the cause, it must be combated and a sufficiency of sleep secured. If pain be very acute, opiates may be necessary and should not be withheld. Omnopon in doses up to $\frac{1}{3}$ grain (0·02) by mouth is very suitable.

Nervous symptoms.—Of these, insomnia is the first in order of appearance; when characterised by insomnia at night and early morning somnolence, it is usually benefited by treatment of the autonomic system with thyroid gland in doses of from $\frac{1}{4}$ to 2 grains (0·015–0·12) t.i.d. p.c.

In certain cases which do not yield to this measure a satisfactory procedure is to give a dose of sulphonal, 15–30 grains (1–2), in the afternoon followed by paraldehyde, 1 drachm (4·0), at bedtime and repeated hourly if required.

Bromide and chloral in 15 grain doses (1·0) are often useful.

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D.A.H.—This, the most obstinate of the nervous manifestations, may appear as early as the beginning of the third week of the disease, and in the management of the acute stage our measures in regard to this complication are chiefly prophylactic. Rest during the febrile stage must again be emphasised.

The use of thyroid gland as recommended for insomnia is found beneficial in all cases in which there is evidence of a disturbance of the autonomic system. The most frequently observed of these are flushing, sweating, cyanosis, vertigo, gastro-intestinal disturbances, general irritability, and well-marked pulsus paradoxus, as evidenced by the marked slowing or even disappearance of the pulse at the wrist when the patient takes a deep breath and holds it for a few seconds. These symptoms, which frequently precede the characteristic, well-marked clinical D.A.H., may be relieved by thyroid and the other measures suggested, the balance of the nervous mechanism restored, until the individual gains the better of the toxin, and the development of the so-called 'effort syndrome' or D.A.H. averted.

Atropin given by mouth has a similar effect, and is often used to reinforce the action of thyroid.

It is our custom to begin with doses of $\frac{1}{200}$ of a grain (0·0003), gradually increasing each day until the physiological effect of the drug is obtained, and then reducing the dose slowly.

These patients vary much, but often need large doses of atropin. It was found necessary, in some cases, to push the drug to a dose as large as $\frac{1}{50}$ of a grain (0·0013) thrice daily before any effect was noted. As a matter of routine atropin is always given one hour or more after each meal, in order to avoid any interference with gastric secretion.

Treatment of the Chronic Disease.—This consists, briefly, in improving the general health and hygienic conditions of

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the individual, with particular attention to rest, exercises, diet, and climatic conditions.

The therapeutic measures recommended in the acute disease are often necessary during relapses, when the symptoms calling for relief may differ but little from those of the primary attack.

The nervous symptoms, including the functional circulatory disturbances recognised in the army as D.A.H., are the factors mainly to be considered in the chronic stage. All that has been said of graded outdoor exercise applies with even more force to this stage of the disease. It must always be remembered, however, that only harm will result if the man be pushed beyond his capacity; he must gradually regain confidence in himself, and this must on no account be shaken by exposing him to the discomfiture of failure. As soon as the disease appears to be quiescent he should be transferred to a convalescent camp near the sea or on a high, or at least dry coast, where he may depend on enjoying a low degree of humidity. The progress made by these cases in such conditions is often quite remarkable.

Close watch must be kept throughout his period of training for any indication of a febrile relapse. During such periods complete rest in bed is essential and must be strictly enforced. Neglect of this precaution aggravates the nervous condition, and is, in addition, the cause of disappointing failure, leading to the loss of confidence already referred to.

A selected diet, rich in anti-beri-beri vitamines, was tried in a group of cases, but these did not show any better result than the cases fed on ordinary hospital diet. A substantial addition of milk to the diet is, however, of advantage.

Many trench fever patients spend much time in hospital on account of concomitant conditions; of these the most

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frequent in our experience are flat or weak feet ; injuries of the feet, pelvic or lumbar muscles ; trench feet ; chronic joint changes ; pyorrhœa alveolaris, and intestinal stasis.

All chronic cases should be carefully overhauled and such causes of disability sought for, and when found met with appropriate measures.

See 'A Treatment for Trench Fever,' by Major J. E. Sweet, M.D., U.S.M.C., and Lieutenant H. B. Wilmer, M.D., U.S.M.C. (*Lancet*, 15.2.19), in which intravenous injections of collargol are shown to give excellent results in both acute and chronic cases. Dose used, 10 c.c. of a 1 per cent. solution of collargol made in sterile distilled water.

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CHAPTER VIII

PROPHYLAXIS

THE prospects of prophylaxis against louse-borne disease are more hopeful than in the case of any other insect-borne malady. In all their stages lice have no normal life apart from their host, and may thus be made the subject of complete control. It is a simple matter to free the individual of lice, and the freeing of the community from them depends upon successful organisation.

Of the three species of lice found upon man *Pediculus humanus*, var. *corporis* (the body-louse), and *Pediculus humanus*, var. *capitis* (the head-louse), are known to be responsible for the conveyance of disease. *Phthirus pubis*, the crab-louse, has not yet been incriminated.

The destruction of lice in civilian life, wherever organised sanitary work exists, should not be a difficult matter. It has become a very important one. Cases of trench fever have occurred in people who have never been out of England, and the possibility of its becoming a common disease here when the armies are demobilised must be borne in mind. Body-lice still exist in considerable numbers in the poorer parts of towns and in agricultural districts, while outbreaks of head-lice are common. Unless great care is taken at demobilisation, lice will certainly increase among us for a time. Such reform in housing conditions as will prevent congestion, and attention to personal hygiene, such as the frequent changing of underclothing, afford the best protec-

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tion against lice and the diseases they convey. History had already proved this before the vector of typhus and relapsing fevers was known, and these maladies had practically disappeared from Western Europe; while it is the country which lags behind in social reform that suffers most from their ravages to-day.

Wherever a case of pyrexia of uncertain origin occurs, the clothing and head of the patient should be carefully examined for traces of lice, and if these are found immediate steps should be taken to disinfest those who have been living in close contact with him, and their bedding. Any of the methods successfully used in the army are available for this purpose. The children in council schools form an excellent index of the incidence of lice among the population, and inspections in schools should be regularly carried out. Cleansing stations are already organised in many large towns, but it is of little use cleansing the child and allowing him to return to an infested home.

The Biology of the Body-Louse

In order to combat lousiness successfully it is necessary that the main features of the biology of the insect should be understood. Lice never originate from dirt, but a dirty condition of life facilitates their increase and spread. The factors which tend most to their increase are the prolonged wearing of underclothing without a change and the wearing of this both by day and night. Because these habits are more pronounced in the winter, lice are more numerous in that season than in the summer months.

Body-lice may occur on any garment inner or outer, and on the body hair, but the large majority are always on the clothing next the skin. When not feeding they tend to congregate along the seams of the garments and to creep

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into crevices. The eggs, or nits, may be laid on any garment or on the body hair. They are usually in clusters and often deeply embedded in seams and folds of the clothing. When the louse has selected a suitable site for oviposition, it returns time after time to the same spot to lay, till an area several inches across may be covered with the eggs, placed a short distance apart. The egg is about a millimetre in length and is firmly fixed, by means of cement at the base, to the fibres of cloth or to hair. The free end is closed by a cap which is pushed off when the egg hatches. The egg is pearly and translucent when newly laid, but becomes more opaque as the young one develops. They are inconspicuous on light-coloured cloth, but the dirty patches of excreta around their site may serve to indicate their whereabouts. The empty shell remains attached long after the louse has emerged, and appears an intenser white than the full egg. Eggs without the cap or those which have turned brown and collapsed are harmless, but it is well to remove them, or they may cause repeated alarm on inspection. Washing the garment does not do this, but in the case of hair, vinegar may be used to loosen them, and they may then be combed off. A pocket lens should be used in deciding the viability of nits.

Lice feed frequently, and mainly on those parts of the body against which the clothing presses closely. They rarely pass on to the skin to feed, but retain their grip on the garment, and merely press the mouth against the skin, the teeth which arm the mouth giving a sufficient grip. As slight movement of the garment would dislodge the mouth, this habit indicates why they feed mostly when their host is at rest, sitting or sleeping, and why they bite little where the clothing hangs loosely. On soldiers the region of the belt is especially favoured by them.

In the act of feeding the soft parts surrounding the mouth, the horseshoe-shaped haustellum and the lower lip,

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form an air-tight cushion against the skin, anchored by means of the recurved hooks or teeth. Into the area thus enclosed the stabbing organ is thrust. Salivary fluid flows into the wound down the salivary pipe which traverses the stabbing organ. After a short interval the louse begins to suck by means of the pumping pharynx, and blood is thus drawn from the wound, not up the centre of the stabbing organ but past it.

The meal is protracted, often lasting for half an hour or more. Generally towards the end of the feed the louse begins to defæcate, but it is not correct to say that it passes out the detritus of its previous meal. There is no continuous motion of the food along the gut as in animals with long narrow alimentary canals. In the louse the food churns to and fro in the wide stomach, and the newly added blood is quickly mixed up with the old partly digested food. Often the fresh blood can be seen to flow past the old detritus so that it passes from the anus almost unchanged, as far as the microscopic appearance of the cells is concerned, though most of the fluid portion is extracted.

The excreta are moist when extruded, but dry very rapidly in the air, so that they fall away from the anus in rough black granular masses or in smooth red fragments. They go into emulsion in sweat very readily, making dirty brown patches on the skin. The excreta collected in bulk have the appearance and colour of finely ground coffee. Fig. 5 shows a fragment of sewing cotton, fouled by louse excreta, removed from one of the experimental boxes. As collected they break up into granules of approximately equal size. An adult louse well fed extrudes about eighty of these granules in twenty-four hours, the weight of these being 0·24 milligram. The female passes rather more than the male. Allowing ten days for the incubation of the virus of trench fever in its body a louse may be infective

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for the last 30 or 35 days of its life, and during this infective period it would extrude nearly 10 milligrams of excreta. Since infection may be produced by 0·1 milligram (Experiment 97), a single louse during its life is capable of producing enough material to infect a hundred men. A man having the trench fever virus in his blood and harbouring 500 lice upon him is the means of producing enough louse excreta daily to infect his whole battalion.

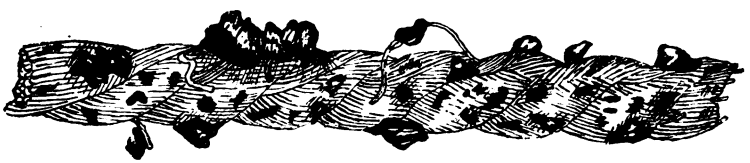

FIG. 5.—Sewing cotton soiled by louse excreta. × 30.

On garments worn continuously the egg hatches on about the seventh or eighth day. The larva becomes an adult after casting its skin three times, at about the third, fifth, and eighth days respectively of its life. The sexes cannot be distinguished in the younger stages except by dissection. The adult female has a broader abdomen than the male, and the tip is slightly forked and turned down. In the male the abdomen is more barrel-shaped, the tip is undivided and turns up. A brown chitinous pointed organ can also be seen in the male through the skin of the ventral side of the abdomen. This is used in dilating the vagina of the female during copulation. (Nuttall.) On the second day after maturity is attained, the female commences to lay eggs, and continues to do so at the rate of about eight to ten a day for some thirty days. In captivity the average life is a little over forty days, but there is occasionally a longevity of fifty days.

From the point of view of the reduction of lice, the most

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important factor in the biology is the length of time which the egg takes to hatch. On garments worn continually very few hatch before the seventh day (Nuttall). This means that if a man is deprived of his body hair so that the lice cannot breed on that, and **obtains once a week a complete clean change of clothing, lice cannot breed upon him.** If this habit becomes general in the community lice of necessity disappear. In the armies, if it were made compulsory for every man to wear long drawers, and he were provided with a clean pair and a clean shirt once a week, while the discarded ones were disinfested, the majority of the lice would be destroyed weekly and immense benefit would accrue. As close an approximation to this ideal as active service conditions will permit should be attempted.

Multiplication of Lice

An extreme case of lousiness, when a man has hundreds on his garments, is the result of his having assumed a very verminous garment, or else of prolonged neglect either through indifference or stress of circumstances. When a man acquires one or two lice only, it takes weeks for this condition to be reached, as will be seen from the following table, which shows the progressive increase through a period of four weeks of the offspring of a single fertile female adult louse. In this is shown the rate of increase on a man who wears his garments continuously, and on the first day of the history acquires a breeding female with the offspring of which he interferes in no way. The figures are based largely on the rate of increase and growth given by Nuttall. The case is of course ideal, since under actual conditions many accidents would befall the eggs and lice, and the numbers would be lower than indicated. It is included here to emphasise the advantage of a weekly change.

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TABLE VII.—Illustrating the Potential Rate of Increase of Lice on Garments continuously worn, showing that a Weekly Change of Clothing with Disinfestation prohibits Louse Breeding, and that Extreme Cases of Lousiness are the Result of Prolonged Neglect.

Day.	Adult Lice.	Eggs.	First Stage Larvæ.	Second Stage Larvæ.	Third Stage Larvæ.	Notes.	Total Lice.
1	1♀	...	...	....	...	.....	1
2	,,	10	...	...	...	.....	1
3	,,	20	...	...	...	.....	1
4	,,	30	...	...	...	.....	1
5	,,	40	...	...	...	.....	1
6	,,	50	...	...	...	.....	1
7	,,	60	...	...	...	.....	1
8	,,	70	...	...	...	.....	1
9	,,	70	10	...	...	Eggs of 2nd day hatch. The man is now liable to infest others.	11
10	,,	70	20	...	...	Eggs of 3rd day hatch.	21
11	,,	70	30	...	...	,, 4th ,,	31
12	,,	70	30	10	...	First Larvæ moult for first time.	41
13	,,	70	30	20	...	.....	51
14	,,	70	30	20	10	First Larvæ moult for second time.	61
15	,,	70	30	20	20	.....	71
16	,,	70	30	20	30	.....	81
17	6♀ 5♂	70	30	20	30	First Larvæ become adult.	91
18	11♀ 10♂	120	30	20	30	First eggs of second generation laid.	101
21	26♀ 25♂	270	30	20	30	.....	131
28	61♀ 60♂	570	80	20	30	First eggs of second generation hatch. Henceforth increase would be rapid.	251

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Dissemination of Lice

Lice which lose contact with their host die of starvation unless they come in contact with a fresh one. The rate of starvation varies with the temperature to which they are exposed. In an ordinary warm room they survive about a week, but at low temperatures they may live for ten days. Eggs may remain alive for a much longer period, since the hatching is retarded by cold. Nuttall records a case where by exposing eggs alternately to warm and cold conditions he delayed their hatching for thirty-five days. It is therefore useless to put off infested garments for a few days, hoping that they will clean themselves. All infested garments should be properly cleansed.

The majority of stray lice probably never find a fresh host, since it is largely by accident that they ever do so. They have no instinct by which they can hunt him down except the attraction of his warmth, and this exerts its influence over a very short distance. The finding of a fresh victim is largely therefore a matter of chance contact. Some lose contact through their own migration, either under warm conditions or when their host becomes, through fever or death, unsuited to them. Most are detached through the garments containing them being discarded or through remaining on blankets when the bed is vacated. Most of these remain where they are in the hope that the garment will be again assumed or the bed reoccupied. A few scatter. The means by which lice may be acquired may be summarised as follows:

(1) Through acquiring a stray louse by coming in contact with it. Stray lice have become detached from their host by:

(*a*) Leaving of their own free will under warm conditions.

(*b*) Migrating when their host has fever.

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(*c*) Migrating when their host is dead.

(*d*) Being detached through brushing or by accident.

(*e*) Leaving discarded garments.

(2) Through sleeping with, or in close contact with, an infested person.

(3) Through sleeping in bedding previously occupied by an infested person.

(4) Through wearing a garment rejected by an infested person if :

(*a*) It has not been treated at all.

(*b*) It has been laundered but not properly disinfested.

(5) Through wearing clean disinfested garments which have been in contact after disinfestation with lousy garments.

(6) Through using articles such as brushes used by an infested person.

Inspection of Troops.—In order to know when disinfestation is necessary frequent inspections should be carried out. In these inspections all the garments should be examined, especially along the seams and at the fork of the trousers or drawers. The hair of the armpits, pubis, and chest should be examined to discover whether lice are harboured in these localities or whether nits are present on the hair. The latter will very often be found, but it is difficult to tell whether they are hatched or fresh without the aid of a lens.

There are also often indications of lousiness on a man's skin though these are not necessarily present. Louse bites vary in appearance. They may be flat rose spots an eighth of an inch across ; slightly raised rose spots like flea bites ; small brown scaly scabs ; small raised hard white shining lumps ; watery blisters like herpes vesicles. Bronze colouration of the skin, more or less extensive, may be present. The dirty brown patches where the louse fæces have emulsified in sweat are also characteristic, especially beneath infested hair.

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Above all, men should be persuaded, and if necessary coerced, to inspect themselves, and to report at once the appearance of lice upon them. We have seen men in hospital with the axillary and pubic hair swarming with lice, and their invariable remark is that if they had known they would have reported it at once. The merest glance, however, would have convinced them of their condition. Without this self-inspection a man may be honestly unaware that he is infested, for many have a remarkable indifference to louse bites which is either natural or acquired. The men should be told that it is not a disgraceful thing to pick up a few lice, but that to retain them is a real danger to their comrades; that they may harbour lice without knowing it unless they look; that it is only by wilful or enforced neglect that they can become very verminous.

In dealing with trench foot in the fighting zone, where formal inspection by the M.O. was impracticable, an institution was set up by which men were made responsible in pairs for one another's feet. Some similar system might be commenced in regard to lice, or a N.C.O. in each platoon should be made responsible for reporting at once to the M.O. each case of infestation as he became aware of it. A small portable disinfesting plant should be at the disposal of every regimental M.O., so that these sporadic cases of lousiness could be dealt with as they arose, with only a brief absence from duty. That men become so verminous in the front line is due mainly to the fact that some members of the unit harbour lice when they leave the training or rest camp. There is now no reason why a division should be allowed to take a single louse from such a place.

Routine Disinfestation of Troops.—In thorough disinfestation—and no system which is not thorough should be considered—it is not enough to allow a man a hot bath and a change of underclothing. The presence of nits and

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lice on the outer garments and on the blankets makes this procedure a palliative measure only. The frequent occurrence of nits on the body hair makes it essential that the person should also receive attention. A hot bath does not destroy these nits. All garments before going to the laundry should be passed through a disinfestor, as the water used for washing is often not of the lethal temperature for lice and the addition of soap makes little difference.

Disinfestation should be so arranged that a man's blankets are treated at the same time as his service dress and underclothing, and while this is being done he should be allowed a hot bath and his person examined in a good light. If nits are seen on the body hair it is advisable to remove this; indeed there can be no question but that a person so placed that he is liable to frequent infestation is in a better position to resist it if he keeps his hair cut very short. In removing the hair care should be taken to avoid abrading the skin, as such abrasions form portals through which the virus of trench fever may enter.

Equally with thoroughness for the man, thoroughness for the unit is necessary. All who share a billet, or come in close contact with one another, should be treated at one and the same time, or the uncleansed will reinfest the cleansed. No man should be allowed to make special duties an excuse for avoiding treatment. A cook or an officer's servant is as likely to be verminous as any other individual.

In the cleansing station care should be taken that treated clothing does not come in contact with that which awaits treatment, nor should it be laid down where uncleansed garments have been. Men should enter at one end, and there strip and pass into the baths. They should receive their treated articles at the other end as they pass out of the baths, so that undressing and redressing should be carried out in separate rooms.

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This routine disinfestation should always be carried out in a division before it leaves the rest or training camp for the front line. All men proceeding on leave should also go through it unless very careful inspection is carried out and they are found free. Casual inspection is quite valueless.

The various methods of destroying lice will be discussed below in brief.

Destruction of Lice by Heat.—No method of louse destruction has been found to supersede heat. This may be applied either as steam or as hot air. While steam is undoubtedly the more effective in destroying the virus of infective louse excreta (see below), it is not found practicable to use it in Europe for armies in the field in the winter months. This is on account of the difficulty of quickly drying the garments for immediate wear—an essential in routine disinfestation of troops. This aspect of prophylaxis has therefore unfortunately to be overlooked, but it should be borne in mind that lousy garments may be dangerous to wear after they have passed through hot-air chambers unless the temperature in these has approached 100° C. The main thing is to destroy the lice which produce the excreta, and to do this in such a way that disinfestation is made as little unpopular as possible among the men.

The degree of heat necessary for the destruction of isolated lice and nits is not great. Nuttall states that hot air of a temperature of 65°–70° C. for one minute, or 58°–61° C. for ten minutes, is sufficient to destroy them. In practice it is necessary to allow a longer time for the penetration of the clothing by the heat. Captain Orr, Canadian A.M.C., recommended exposure at 60°–65° C. for fifteen minutes as a working basis. The time allowed should be calculated from the moment when these temperatures are attained, and not from that when the hot chamber is closed up. Where these low temperatures are employed, it is necessary that the

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machine should be provided with a thermometer. The heat of the atmosphere in a hot-air chamber is not the same in all parts. The neighbourhood of the walls and roof is cooler than the centre, so that the articles should not be hung on the walls, but on a central rack. Garments should be turned inside out and hung loosely; blankets should not be folded, but festooned over pegs. Overloading of a chamber should be avoided.

As much time is lost and heat wasted in loading and unloading large chambers, through waiting for them to cool sufficiently to be entered, all types should be provided with trolleys on which the clothes may be hung and which may be wheeled in. These should be provided in duplicate, so that one may be unloaded and again loaded while the other is in the chamber. Of the numerous types of disinfestor which have been devised, a few are briefly described below.

The Disinfestation Train, much used in Egypt, consists of an engine to supply the steam and an ordinary iron goods van. The van is fitted with shelves, and into it the steam is led from the engine. The clothing to be treated is tied in bundles in the blankets and packed on the shelves. As superheated steam is used, the heat penetrates right through the bundles, and, according to Hunter, a temperature of 105° C. is attained in the centres. No attempt is made to make the van air-tight. The operation continues for an hour after the steam is turned on. Owing to the superheating the articles are almost dry when withdrawn. Other advantages of this device are that it combines a large capacity with its mobility. A similar arrangement for roads could doubtless be constructed from a steam tractor and a pantechnicon.

The Serbian Barrel was devised by Lieutenant-Colonel G. F. Stammers, R.A.M.C., to deal with the epidemic of

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typhus fever in Serbia in 1915. It consists of an ordinary sixty-gallon wine barrel provided with a tightly fitting lid. The bottom is perforated with a number of large holes, and a little above this is a grid of wire or wood on which the load of four kits rests. This is placed over a boiler consisting of a large petrol tin, a sand-bag collar intervening to conserve the steam. A furnace is improvised around the base. After steam issues freely round the lid the load is left in for half an hour. A similar arrangement may be made out of an ordinary galvanised-iron sanitary bin. A foot of water is placed in it, and over this is a wire grid. The whole is placed over a furnace. The advantages of these are their cheapness, their simplicity, and their portability. One or two should be enough to deal with sporadic cases of lousiness which may crop up in a battalion when it is impracticable to take the men in a body to a larger and more elaborate disinfesting station.

The Russian Pit consists of a large chamber dug in the ground, roofed by corrugated iron and heavily earthed over. Steps lead down into this, and the entrance is closed by a sliding door. Racks are arranged in the centre of the chamber for the garments being treated. Two braziers of coke are placed in opposite corners of the chamber, and from these chimneys lead up through the roof. If the air which percolates into the chamber past the door is insufficient for combustion, pipes are led from the stairway to open under the braziers.

Such a device is easy to construct and to work, but is necessarily slow in operation.

The Canadian Hot-Air Chamber, devised by Captain Orr, is built of corrugated iron over a pit. The walls are double, and the intervening space is filled with clay to conserve the heat. A thick layer of earth is placed over the roof. One side of the chamber is closed by tightly fitting doors.

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The floor is of corrugated iron and is perforated by numerous holes except in that part which is immediately over the two braziers which are placed in the pit below. A thermometer is built into the wall of the chamber so that it may be read from outside. The articles to be treated are loosely hung on racks which run in and out of the chamber on rails. These rails run both to the exit and the entrance of a bath-house. One carrier is loaded with untreated clothing at the entrance while the second carrier of clothing is being treated. Treatment is complete after the temperature has been maintained at 75° C. for twenty minutes, and the load is then run to the exit of the bath-house to be unloaded. The one ready loaded and awaiting treatment is then at once thrust into place in the chamber. A temperature of over 80° C. is sometimes attained, but the heat under the folds of the blankets lags somewhat behind this, though still sufficient for the destruction of the vermin. This is probably the most economical disinfestor yet devised. It has the further advantage that it is simple to construct, and that the necessary materials are generally to hand even in the field.

Other Methods of Disinfestation.—**Lysol** in 2 per cent. solution, at a temperature above blood heat, *i.e.* at about 40° C., will destroy all lice and nits on garments soaked in it for half an hour. If the temperature is lower than this, though the nits are all killed, some of the lice may revive, even after the space of twelve hours of apparent death. When killed by this means lice rapidly turn black. This process also renders the infective excreta harmless (Experiment 74), and is therefore a convenient method of treating the garments of trench fever cases on admission to hospital.

Sulphur dioxide has been recommended at various times as an alternative to heat for louse destruction. After discussing the evidence relating to this, Nuttall states:

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'It appears to my unbiassed judgment that the foregoing evidence sufficiently condemns SO_2 as a means of destroying lice. It is shown that it is untrustworthy, injurious to uniforms, slow in action, unduly costly and wasteful. The slowness of the process makes it impossible for the soldier to resume his clothing promptly after a bath, as in the case of hot-air or steam disinfestation.'

Ironing the garments by means of heavy hot irons is a palliative method of disinfestation. Alternatively the clothing may be pressed against hot iron plates. In ironing, the instrument should be made to linger along the seams, which should be opened out. It cannot be considered a radical method, as it is almost impossible to ensure the death of every louse and nit. Nevertheless considerable relief may be given by this means, and it is well worth adopting when proper disinfestors are unavailable.

Repellants.—Among the numerous substances which have been recommended from time to time as repellants, the one which appears best to have withstood the test of time and practicability is naphthalene, alone or in combination. Bacot showed that the radius of action of a repellant is very small, so that treated belts or sachets merely protect that part of the body in their immediate neighbourhood. In using a repellant substance it is therefore necessary to treat the entire covering of the body. Lice dislike grease, which runs over their bodies and chokes them by clogging the breathing pores. Any greasy substance is to some extent beneficial in its action.

Bacot and Copeman recommended a mixture of four parts of crude unwhizzed naphthalene from the coke oven with one part of soft-soap. It is necessary to smear it over the entire inner surface of the clothing which comes in contact with the skin.

N.C.I. (naphthalene 96 parts, creosote 2 parts, and iodo-

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form 2 parts) is a powder which was favourably reported on by Peacock, who subjected it to practical tests in the field. He recommends that it should be dusted all over the inner side of the garments, the repellant action lasting for a few days.

It is strongly advised that any worker whose duty it is to handle the sick or their effects before disinfestation, during any louse-borne epidemic, should use one or other of these substances. The liability of such people to contract these diseases has always been a remarkable feature of the epidemics. They are also recommended for the soldier when he is so placed that other methods of disinfestation are impracticable.

Disinfestation of the Sick.—Lice are very sensitive to changes of temperature, and the increase of heat on the skin during fever causes them discomfort. This very greatly increases their migration even if the temperature of their host does not rise above 100° F., so delicately are they adapted to the normal condition. This habit accelerates the spread of epidemics of louse-borne diseases, since the lice which thus migrate are the infected ones. Sick and wounded among the armies should therefore be segregated as early as possible, and the fever cases should be freed from lice before they are again mingled with other casualties. Those handling the sick and their discarded garments should take special precautions to avoid getting the lice upon them. Either louse-proof overalls or some louse repellant should be used.

Whenever practicable, steam chambers should be used in preference to hot-air chambers for the cleansing of these effects. The underclothing may with advantage be steeped in a hot 2 per cent. solution of lysol before being laundered. The louse excreta are thus rendered harmless, and no danger is incurred in again issuing the clothing to others.

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Since, by the findings of the American Trench Fever Commission, the urine and sputum of the patients may convey infection, they recommend that these should be sterilised.

The Destruction of the Virus in the excreta of trench fever infected lice.—It must be remembered that in dealing with epidemics of trench fever not only the insects which are infected are dangerous, but also the excreta which they have extruded during their infected period. While much of this is shed and blown about in the air, much also clings to the fabric of the garments. Any one, therefore, assuming garments containing such excreta renders himself liable to an attack of the disease through this coming in contact with abrasions of the skin. For this reason, whatever process of disinfestation is adopted, it should, while it destroys the lice and their eggs, also render the infected excreta harmless. It is highly probable that this remark applies to typhus equally with trench fever.

Longevity of the trench fever virus in louse excreta.—That the virulence of the trench fever infected excreta is retained for at least four months, and probably much longer, since its infectivity was in no way reduced in this period, is shown by the following three experiments :

Experiment 21.—Doolan, a healthy man, was inoculated by scarification with excreta of proved virulence which had been kept at room temperature in sunlight for **sixteen days.** The excreta were the product of many lice infected from various sources. Eight days later he developed a typical attack of trench fever.

Experiment 57.—Beever, a healthy man, was inoculated by scarification with excreta known to be infective when fresh, which had been kept at room temperature in glass tubes plugged with cotton wool for **sixty-one days.** The excreta were the product of many lice infected from various

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sources. Seven days later he developed a typical attack of trench fever

Experiment 95.—Heyne, a healthy man, was inoculated by scarification with excreta of proved virulence which had been kept in plugged tubes at room temperature for **one hundred and twenty days.** The excreta were the balance of those used in the previous experiment. Thirteen days later he developed a typical attack of trench fever.

Further evidence that the infective excreta remains virile for very long periods after it has left the louse is afforded by a number of experiments in which excretá were used which had been passed long before the time when they were inoculated. In this connection reference should be made to the tables in Appendix I giving the data of the experiments. The age of the excreta used is given in each case.

The Effect of Laundry Processes on the trench fever virus in louse excreta.—Since the virus in the blood of trench fever patients is destroyed by distilled water in large quantities, an experiment was conducted to discover whether the ordinary laundering processes would render the excreta harmless. It was found that **immersion in hot soapy water for twenty minutes did not reduce the virulence,** and that therefore some precaution other than the mere washing of the garments must be carried out.

Experiment 75.—The excreta used were of an infectivity proved by Experiment 64. The most recent of the excreta were three days old when treated. 200 c.c. of a 2 per cent. solution of ordinary army yellow washing soap in tap water were heated to a temperature of 50° C. and allowed to cool to 47° C., this being a temperature at which washing by hand could be comfortably done. About 20 milligrams of the excreta were tied in a linen bag and immersed in the solution, and pressed till thoroughly wetted through. They were kept in the solution for 20 minutes,

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during which time the temperature fell to 38° C. The bag was then removed and opened, and allowed to dry at room temperature under sterile conditions. Four days later part of the excreta was inoculated by scarification into Raine, a healthy man, who ten days later developed a typical attack of trench fever.

The Effect of Standard Disinfectants on the trench fever virus in louse excreta.—The effects of two standard disinfectants, lysol and liquor saponatus cresoli fortis, on infective excreta were investigated in the two following experiments. **It was found that the excreta were rendered harmless by immersion in lysol or cresol in 2 per cent. solution for twenty minutes at room temperature.**

Experiment 74.—Inoculation with infective excreta treated by a solution of lysol.—The excreta used were from the same source as those in Experiment 75, which gave a positive result. The most recent were two days old when treated. About 20 milligrams of the excreta were tied in a linen bag and immersed in 60 c.c. of a 2 per cent. solution of lysol in tap water at a temperature of 20° C. The bag was squeezed to expel the air, and was left immersed for 20 minutes. It was then opened, drained on clean filter paper, and allowed to dry at room temperature under sterile conditions. Two days later part of the dried excreta was inoculated by scarification into Heyne, a healthy man, no effect resulting during 25 days' observation. Heyne was then shown to be non-immune to trench fever by Experiment 95.

Experiment 80.—Inoculation with infective excreta treated by a solution of liquor saponatus cresoli fortis.—The excreta used, the time of immersion, and the *modus operandi* were as in Experiment 74. A 2 per cent. solution was employed at T. 18·5° C. Seven days after treatment part of the dried excreta was inoculated by scarification into Hicks, a healthy man, no effect resulting during 25 days' observation.

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A series of experiments was conducted to determine the degree of heat necessary for the destruction of the virus during disinfestation, especially whether that ordinarily used was sufficient for this purpose. Since both wet and dry heat have been used for louse destruction, the effect of each was tested on the excreta. The heating operations were carried out in collaboration with Bacot at the Lister Institute of Preventive Medicine. The apparatus used (Fig. 6) consisted of a large water-bath provided with a gas regulator (C), and with the water surface covered by a layer of liquid paraffin. In this a conical flask was immersed up to the neck. When the effects of dry heat were being tested, the flask was empty and the cork was provided with ventilation holes loosely plugged with cotton wool (B). In testing the effects of wet heat the flask contained a little water and the cork was entire, so that the atmosphere inside was saturated with moisture. A thermometer, tested against a Kew Standard Thermometer, was passed through the cork. When this had registered steadily the degree of heat required, the excreta, about 20 milligrams, suspended in a muslin bag (A) were placed in the flask against the bulb of the thermometer. The excreta were not ground in these tests, so that the conditions should approach as nearly as possible to those of routine disinfestation of clothing. The time allowed in the treatment was calculated from the moment when the correct temperature was again recorded; a matter of two or three minutes after the excreta were placed in the flask. The thermometer was read frequently throughout the process, the fluctuations of temperature being very small. The effect of the treatment was in each case tested by the inoculation of a healthy volunteer. The details of the experiments follow.

Experiment 33.—Inoculation with infective excreta heated at 56° C. for 20 minutes. Dry heat.—The excreta used were

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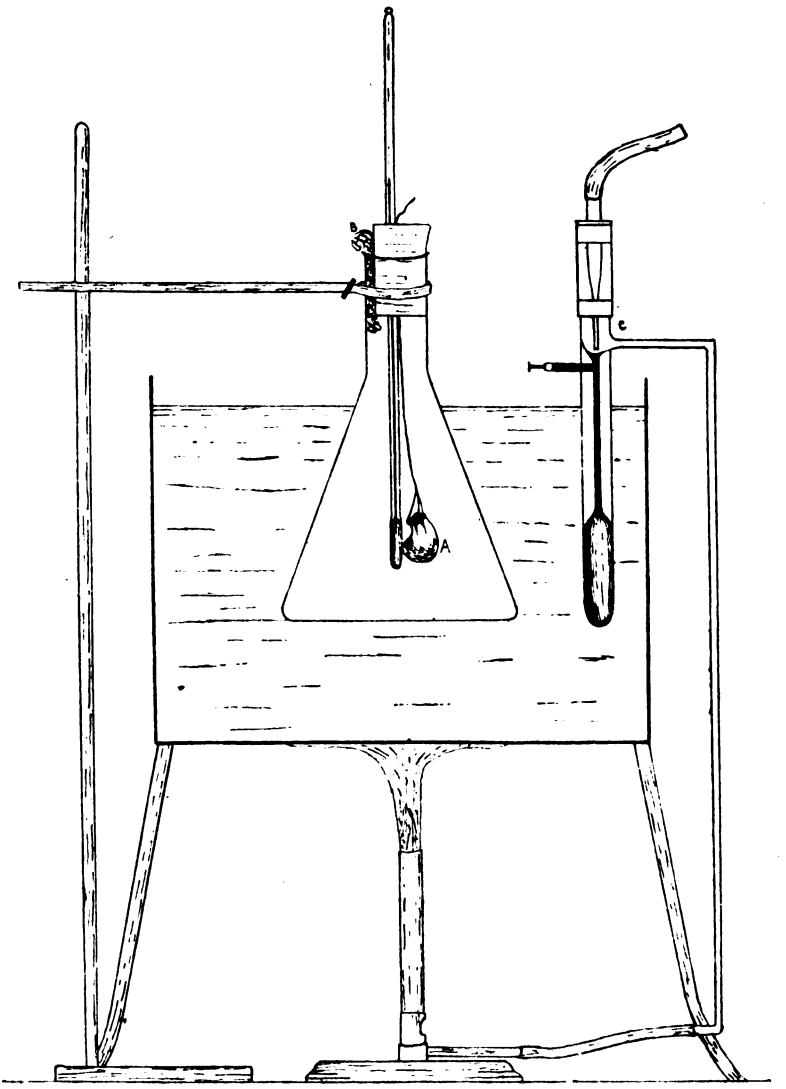

FIG. 6.—Diagram of apparatus used for the heating of louse excreta.

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a mixture collected from many trench fever infected lice during the 40 days previous to the experiment. Jones, a healthy man, was inoculated by scarification on the day of the treatment and on the two successive days following; the excreta being kept in the meantime in a sterile tube plugged with cotton wool. Eight days after the first inoculation he developed a typical attack of trench fever.

Experiment 58.—Inoculation with infective excreta heated at 65° C. for 20 minutes. Dry heat.—The excreta used were collected from 1000 trench fever infected lice, on the 9th, 10th, and 11th days after the infection, the most recent being collected 10 days before treatment. Four days after treatment part of the excreta was inoculated by scarification into Evans, a healthy man. Twelve days after inoculation he developed a typical attack of trench fever (Chart 43).

Experiment 73.—Inoculation with infective excreta heated at 70° C. for 20 minutes. Dry heat.—The excreta used were from the same source as those used in Experiment 75 above, the most recent being collected 7 days before treatment. Five days after treatment part of the excreta was inoculated by scarification into Murray, a healthy man. Nine days after inoculation he developed a typical attack of trench fever (see Chart 27).

Experiment 84.—Inoculation with infective excreta heated at 80·5° C. for 20 minutes. Dry heat.—The excreta used were from the same source as those used in Experiment 75 above, the most recent being collected the day before treatment. Two days after treatment part of the excreta was inoculated by scarification into Syred, a healthy man. Eight days after inoculation he developed a typical attack of trench fever.

Experiment 94.—Inoculation with infective excreta heated at 100° C. for 20 minutes. Dry heat.—The excreta used were from the same source as those used in Experiment 75

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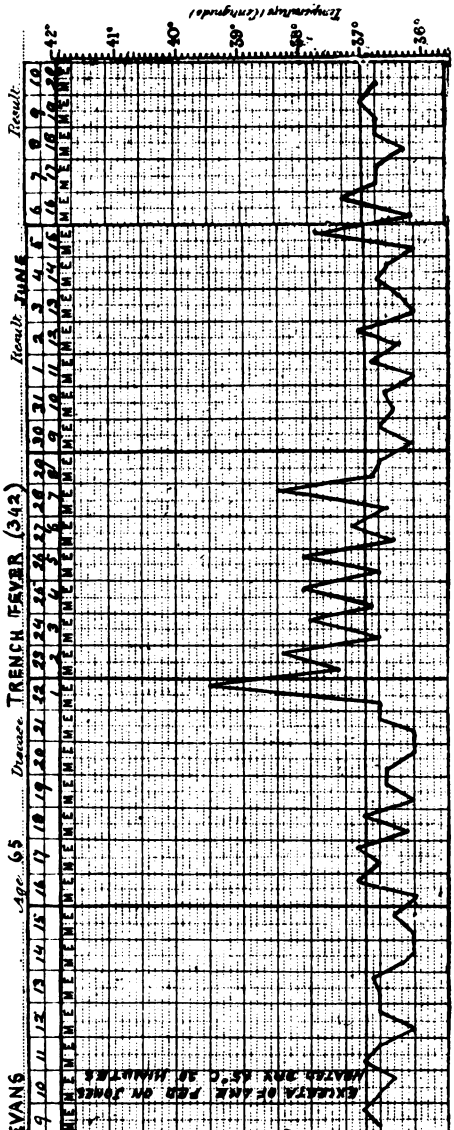

CHART 43.—The result of infection with trench fever louse excreta heated with dry heat for twenty minutes at 65° C.

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above, the most recent being collected seventeen days before treatment. Two days after treatment part of the excreta was inoculated by scarification into Chilvers, a healthy man, no effect resulting during 25 days' observation. That the excreta used were virulent before the heating is proved by the positive results following its inoculation in Experiments 74, 75, 77, 73, and 84.

Experiment 34.—Inoculation with infective excreta heated at 80·5° C. for 10 minutes. Wet heat.—The excreta used were as in Experiment 33 above, the most recent being collected the day before treatment. Part of the excreta was inoculated by scarification into Howlett, a healthy man, on the day of the treatment and on the two successive days following; the excreta being kept in the meantime in a sterile tube plugged with cotton wool. No effect resulted during 25 days' observation. Howlett was then shown to be non-immune to trench fever by Experiment 59. That the excreta used were virulent before treatment is proved by the positive results following its inoculation in Experiments 32 and 33.

Experiment 82.—Inoculation with infective excreta heated at 70° C. for 20 minutes. Wet heat.—The excreta used were from the same source as those used in Experiment 75 above, the most recent being collected the day of treatment. Two days after treatment part of the excreta was inoculated by scarification into Mitchell, a healthy man, no effect resulting during 35 days' observation. He was then shown to be non-immune to trench fever by Experiment 97. (For evidence of virulence of excreta before treatment, *vide* Experiment 94.)

Experiment 83.—Inoculation with infective excreta heated at 60° C. for 20 minutes. Wet heat.—All details, with the exception of the degree of heat used, were as in the previous experiment. Part of the excreta was inoculated by

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scarification into Hanlon, a healthy man, no effect resulting during 35 days' observation. He was then shown to be non-immune to trench fever by Experiment 96. (For evidence of virulence of excreta before treatment, *vide* Experiment 94.)

A summary of the foregoing experiments is given in Table VIII.

TABLE VIII.—SHOWING THE DEGREE AND QUALITY (WET OR DRY) OF HEAT NECESSARY TO DESTROY THE VIRUS IN THE EXCRETA OF TRENCH FEVER INFECTED LICE.

Number of Experiment.	Temperature.	Wet or Dry Heat.	Duration of Treatment.	Result of Subsequent Inoculation.
33	56° C.	Dry	20 minutes	Positive
58	65° C.	Dry	20 ,,	Positive
73	70° C.	Dry	20 ,,	Positive
84	80·5° C.	Dry	20 ,,	Positive
94	100° C.	Dry	20 ,,	Negative
34	80·5° C.	Wet	10 ,,	Negative
82	70° C.	Wet	20 ,,	Negative
83	60° C.	Wet	20 ,,	Negative

The American Red Cross Commission on Trench Fever found that the virulence of the excreta was not destroyed by exposure to 60° C., wet heat, for 30 minutes, but that it was destroyed by exposure to 70° C., wet heat, for 30 minutes. We are unable to account for this discrepancy.

The degree of heat usually employed in the hot air disinfestation plants is therefore insufficient to render the excreta harmless, and disinfestation by means of steam must be considered the ideal method where louse-borne disease exists. For reasons stated above it is not practicable to use steam for the armies in the field in Europe, but it might be used with advantage for the treatment of the clothing of those admitted to hospital. The heat in hot air chambers should be as great as may be used with safety.

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APPENDICES

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APPEN

1.—BLOOD TRANSMIS

Experiment Number.	Name.	T.F. Number.	Age.	Date of Coming Under Observation.	Date of Experiment.	Nature of Experiment.	Result.	Source of Infection.		Interval between Collection and Experiment.	Treatment of Inoculum.
								Name and Number.	Day of Disease.		
3	Robinson, E.	238	70	5.1.18	13.1.18	Whole blood intravenously	+	Kelly (258)	24	8 mins.	Citrated
4	Bryant, T.	267	71	16.1.18	22.1.18	Whole blood i.v.	+	Bligh (269)	9	5 mins.	Citrated
5	Carpenter, W. H.	268	43	16.1.18	22.1.18	Laked whole blood i.v.	–	Bligh (269)	9	1 h. 45 m.	Added to 170 c.c. Aq. Dist. and Saline
6	Woollard, V.	249	24	5.1.18	22.1.18	Laked and filtered blood i.v.	–	Bligh (269)	9	1 h. 30 m.	Do., filtered
7	Jordan, C.	299	66	2.2.18	4.2.18	Whole blood i.m.	–	Robinson (238) Exp. 3	3	½ minute	Citrated
15	Ward, J.	361	50	20.2.18	27.2.18	Whole blood i.v.	+	Reynolds (345)	2	1 minute	Citrated
16	Harlow, G.	364	69	20.2.18	27.2.18	Serum i.v.	–	Reynolds (345)	2	3 h. 25 m.	15 m. centrifuging after clotting
19	Jordan, C.	299	66	2.2.18	13.3.18	Whole blood i.m.	+	Tyler (373)	51	1 minute	Citrated
36	Woollard, V.	249	24	16.1.18	15.4.18	Whole blood i.v.	+	Jones, G. (380)	2	1 minute	Citrated
38	Evans, G.	362	65	20.2.18	15.4.18	Scarification with whole blood	–	Jones (380)	2	1 minute	
44	Stephens, C.	420	66	20.3.18	23.4.18	Scarification with dried blood	–	Jones (380)	2	8 days	Dried at room temperature
87	Libby, J.	638	43	10.6.18	18.6.18	Whole blood i.v. Min. quantity	+	Raine (623)	1	1 minute	Citrated
88	Donnelly, T.	643	70	12.6.18	18.6.18	Scarification with whole blood	–	Raine (623)	1	1 minute	Citrated
124	Bewers, E.	866	17	2.9.18	12.9.18	Whole blood i.v. Min. quantity	–	Finnis (852)	1	1 minute	Citrated, equal parts
135	Devine, H.	625	26	5.6.18	25.9.18	Whole blood i.v.	+	Smale (874)	1	1 minute	Citrated 2 c.c. 1·8 % sod. cit. sol.
136	Brown, W.	884	74	19.9.18	25.9.18	Laked whole blood i.v.	+	Smale (874)	1	17 mins.	Citrated. Laked in 20 c.c. distilled water, 6 mins. made isotonic, 5× N.S.
137	Oldfield, J.	888	62	19.9.18	27.9.18	Dried T.F. blood subcut.	–	Smale (874)	1	42 hours	Dried over H_2SO_4 for 39½ hours
139	Langley, W.	626	28	6.6.18	25.9.18	Whole blood subcut.	–	Smale (874)	1	3 mins.	Citrated in 2 c.c. 1·8 % sod. cit. sol.

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DIX I

SION EXPERIMENTS

Dosage. No. of Lice. C.C. of Blood. C.C. of Urine.	Site of Inoculation.	Interval in Days between Infection of Lice and Passage of Excreta.	Incubation Period.	Type of Attack.	Date of Discharge.	Summary of Previous Experiments.	Remarks.
5 c.c.	Vein		19	E. 10 days fever. Shin pain	6.3.18		Marked arrhythmia.
5 c.c.	Vein		5	B. Relapse 7th, 8th days	6.3.18		Spleen palpable.
2·7 c.c.	Vein				20.2.18		
3·2 c.c.	Vein				20.2.18		
5 c.c.	Right buttock				13.3.18		
5 c.c.	Vein		5	D. 48 days of irregular fever	29.4.18		Blood transmission of excreta infection.
4·5 c.c.	Vein				6.4.18		
5 c.c.	Right buttock		8	Afebrile. One relapse	29.4.18	7. Whole blood intramusc., neg.	Attack proved T.F. by Exp. 56.
5 c.c.	Vein		7	D. Relapsing to 38th day	9.6.18	6. Filtered laked blood, neg. 23. Excreta of lice fed on T.F. patient 24 hours previously, neg.	Control to Exp. 38, 39, 41, 42, 43, 44, 45, 46, 52, 53, 54, 55.
10 c.mm.	Skin				10.5.18	13. T.F. louse excreta by mouth, neg.	
1 c.c.	Skin				18.5.18	25. Excreta of lice fed on T.F. patient five days previously, neg.	
0·5 c.c.	Vein		7	B. Mild. Febrile relapse 7th day without symptoms	20.7.18		
0·5 c.c.	Skin				18.7.18		
0·1 c.c.	Vein				7.10.18		
5 c.c.	Vein		7	B.	14.10.18	78. Scarification with urine, neg. 106. Gut of louse. Rickettsia neg., Res. neg.	Control to Exp. 136, 137 and 139.
5 c.c.	Vein		10	B.	24.10.18		Smale, Exp. 127.
5 c.c.	Subcut. dry				22.10 18		Weight of dry blood 1·0985 grms.
5 c.c.	Subcut.				21.10.18		Control to Exp. 137.

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2.—LOUSE FEEDING

Experiment Number.	Name.	T.F. Number.	Age.	Date of Coming Under Observation.	Date of Experiment.	Nature of Experiment.	Result.	Source of Infection.		Interval between Collection and Experiment.	Treatment of Inoculum.
								Name and Number.	Day of Disease.		
1	Cole, W. H.	233	64	29.12.17	4.1.18	T.F. louse feeding	–	Various		3 to 6 h.	
2	Edgeler, H. H.	234	78	29.12.17	5.1.18	T.F. louse feeding	–	Various		20 m. to 6 h.	
40	Riches		28	19.1.18	29.3.18	T.F. louse feeding	–	Various			
47	Prince, A.	453	44	9.4.18	15.4.18	T.F. louse feeding	–				
48	Jackson, R.	454	54	9.4.18	15.4.18	T.F. louse feeding	+	Various			
50	Bell, E.	612	29	21.3.18	18.4.18	T.F. louse feeding	–	Various			
67	London, W. R.	Malaria	28		14.5.18	T.F. louse feeding, 5 days	–	Various			
68	Barnett, O.	Malaria	21	12.4.18	14.5.18	T.F. louse feeding, 35 days	+	Various			

3.—INOCULATIONS WITH

17	Howlett, R.	379	67	6.3.18	12.3.18	Excreta clean lice	–	Bacot's stock		17½ hours	
18	Jones, G.	380	68	6.3.18	12.3.18	Excreta clean lice	–	Bacot's stock		17½ hours	

4.—INOCULATIONS WITH EXCRETA

(*A*).—

8	Sullivan, D.	298	64	2.2.18	5.2.18	Excreta of T.F. lice	+	Various		6 hours	
10	Reynolds, G.	345	68	13.2.18	19.2.18	Excreta of T.F. lice	+	Various		15 mins.	
11	Tullett, R.	320	60	8.2.18	19.2.18	Excreta of T.F. lice	+	Various		15 mins.	
12	Glover, R.	321	28	8.2.18	19.2.18	Excreta of T.F. lice	+	Various		1 h. 15 m.	
32	Harlow, G.	364	69	20.2.18	6.4.18	Excreta of T.F. lice	+	Various		3 hours	
56	Goodman, H.	569	52	3.5.18	7.5.18	Excreta of T.F. lice	+	Jordan (299)	8th to 16th	27 days	
64	Smith, J.	595	60	14.5.18	20.5.18	Excreta of T.F. lice	+	Steer (484)	27 and 28	1 hour	
72	Simpson, T.	568	74	3.5.18	1.6.18	Excreta of T.F. lice	+	Tovey (16)	*298-339*	1 day	
81	Sherman, E. C.	628	26	8.6.18	14.6.18	Excreta of T.F. lice	+	Steer (484)	27 and 28		Finely ground (Barnard)
92	Morris, S.	668	34	17.6.18	22.6.18	Excreta of T.F. lice	–	Tovey (16)	298-339	21 days	
93	Oldbury, J.	669	24	17.6.18	22.6.18	Excreta of T.F lice	–	Tyler (374)	116-118	19 days	
96	Hanlon, J.	640	76	12.6.18	19.7.18	Excreta of T.F. lice	+	Arkwright	9		Dissolved in 1 c.c. N.S. and allowed to stand 1 h.

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EXPERIMENTS

Dosage. No. of Lice. C.C. of Blood. C.C. of Urine.	Site of Inoculation.	Interval in Days between Infection of Lice and Passage of Excreta.	Incubation Period.	Type of Attack.	Date of Discharge.	Summary of Previous Experiments.	Remarks.
9,518 bites	Skin				19.3.18		Lice proved infective, Exp. 8.
13,224 bites	Skin				13.3.18		Lice proved infective, Exp. 8.
4,945 bites	Skin				7.5.18		
23,821 bites	Skin				7.5.18		Lice fed directly on the skin.
25,609 bites	Skin		14	E. Febrile to 35th day	10.6.18		Lice fed through chiffon.
21,908 bites	Skin				17.6.18		Acute febrile tonsilitis, 21.5.18. (33rd day).
7,520 bites	Skin				10.6.18		Skin washed abs. alcohol after feeding. Not less than 6000 infected bites.
40,580 bites	Skin		35	B. Febrile relapse 5th and 6th days	18.7.18		Skin washed abs. alcohol after feeding.

EXCRETA OF CLEAN LICE

300 lice	Skin				6.4.18		
300 lice	Skin				6.4.18		

OF TRENCH FEVER INFECTED LICE

VARIOUS.

576 lice	Skin	6 h. to 27 days	8	B. Relapse 6th, 7th, 8th days. Mild	13.3.18		
	Skin	Up to 35 days	7	D. Fever to 26th day. Severe	9.4.18		Blood infective 7th day. See Exp. 15.
	Skin	Up to 35 days	8	A. No relapse	23.4.18		Immune 30th day of disease.
	Skin	Up to 35 days	9	C. Two relapses	23.4.18		Immune 31st day of disease.
	Skin		8	B. Relapse 6th, 7th, 8th days	13.5.18	16. Unfiltered T.F. serum, neg.	Control to Exp. 33 and 34.
	Skin		7	E. 12 days irregular fever	29.5.18		Jordan (Exp. 19) T.F. attack afebrile throughout.
	Skin	11 to 13	7	C. Typical	17.6.18		*Steer afebrile when lice fed.*
300 lice	Skin	Up to 41	10	C. Mild. Relapse 6th, 7th, 8th and 11th, 12th days	26.6.18	54. Excreta from lice infected 6 days previously	Tovey, neurasthenic symptoms.
500 lice	Skin		10	C. Prolonged relapsing	19.8.18		Infectivity proved, Exp. 64.
300 lice	Skin	11 to 24			18.7.18		Repetition of Exp. 72.
250 lice	Skin	14 to 17			9.7.18		Lice fed on Tyler prior to Exp. 65.
2 mgm.	Subcut.	8 to 22	7	E. 'Saddleback'	19.8.18	83. Excreta heated moist 60° C. 20 minutes	

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4.—INOCULATIONS WITH EXCRETA OF

(*A*).—

Experiment Number.	Name.	T.F. Number.	Age.	Date of Coming Under Observation.	Date of Experiment.	Nature of Experiment.	Result.	Source of Infection. Name and Number.	Source of Infection. Day of Disease.	Interval between Collection and Experiment.	Treatment of Inoculum.
97	Mitchell, E.	641	70	12.6.18	19.7.18	Excreta of T.F. lice	+	Arkwright	9		Same as Exp. 96, diluted 1 in 10
102	Chilvers, R.	722	62	26.6.18	30.7.18	Excreta of T.F. lice	-	Arkwright	9		Dissolved in 1 c.c. N.S. and allowed to stand 2 hours. Injected subcut.
109	Chilvers, R.	722	62	26.6.18	24.8.18	Excreta of T.F. lice	-	Arkwright	9		1 mgm. excreta dissolved in 10 c.c. N.S. after drying and grinding
130	Chilvers, R.	722	62	26.6.18	20.9.18	Excreta of T.F. lice	-	Arkwright	9	70	

(*B*).—SHOWING INTERVAL BETWEEN INFECTING

23	Woollard, V.	249	24	16.1.18	21.3.18	Excreta of T.F. lice	-	Gatehouse (347)	79	45 mins.	
24	Carpenter, W. H.	268	43	16.1.18	23.3.18	Excreta of T.F. lice	-	Gatehouse (347)	79		
25	Stephens, C.	420	66	20.3.18	25.3.18	Excreta of T.F. lice	-	Gatehouse (347)	79		
26	Stanton, M.	422	67	20.3.18	28.3.18	Excreta of T.F. lice	-	Gatehouse (347)	79		
27	Buchanan, J.	421	75	20.3.18	1.4.18	Excreta of T.F. lice	+	Gatehouse (347)	79		
30	Woodhams, G.	391	63	14.3.18	13.4.18	Excreta of T.F. lice	+	Gatehouse (347)	79	24 hours	

(*C*).—SHOWING INTERVAL BETWEEN INFECTING FEED

29	Barnaby, C.	452	66	9.4.18	17.4.18	Excreta of T.F. lice	-	Jones (380)	2 and 3		
53	Williams, T.	565	76	3.5.18	7.5.18	Excreta of T.F. lice	+	Jones (380)	2 and 3	17 days	
41	Cleary, T.	451	75	9.4.18	21.4.18	Excreta of T.F. lice	-	Jones (380)	2 and 3		
54	Simpson, T.	568	74	3.5.18	7.5.18	Excreta of T.F. lice	-	Jones (380)	2 and 3	16 days	
42	Carpenter, D. H.	268	43	16.1.18	22.4.18	Excreta of T.F. lice	+	Jones (380)	2 and 3		
55	McDonnell, D.	566	70	3.5.18	7.5.18	Excreta of T.F. lice	+	Jones (380)	2 and 3	15 days	
43	Stanton, M.	422	67	20.3.18	23.4.18	Excreta of T.F. lice	-	Jones (380)	2 and 3		

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TRENCH FEVER INFECTED LICE—*continued*

VARIOUS—*continued*

Dosage. No. of Lice. C.C. of Blood. C.C. of Urine.	Site of Inoculation.	Interval in Days between Infection of Lice and Passage of Excreta.	Incubation Period.	Type of Attack.	Date of Discharge.	Summary of previous Experiments.	Remarks.
0·1 mgm.	Sub-cut.	8 to 22	11	C. Relapses 7th and 13th days	26.8.18	82. Excreta heated moist 70° C. 20 mins.	
0·05 mgm.	Sub-cut.	8 to 22			24.8.18	94. T.F. louse excreta heated 100° dry for 20 mins.	Same sample of excreta used in Exp. 96, 97 and 102.
0·1 mgm. in 1 c.c.	Sub-cut.	8 to 22			26.9.18	94. T.F. louse excreta heated 100° dry 20 minutes, negative. 102. 0·05 mgm. T.F. louse excreta subcut., negative.	Same louse excreta used for Exp. 96, 97, 102, 109.

FEED AND INFECTIVITY OF EXCRETA

500 lice	Skin	1			15.4.18	6. Laked and filtered blood i.v., negative.	
400 +	Skin	3			22.4.18	5. Blood laked with distilled water, negative.	Lice fed on healthy men after first 24 hours.
400 +	Skin	5			23.4.18		Lice fed on healthy men after first 24 hours.
400 +	Skin	8			23.4.18		Lice fed on healthy men after first 24 hours.
	Skin	12	8	3. One relapse 10th, 11th days	29.5.18		Lice fed on healthy men after first 24 hours. Œdema both legs 25th day of disease.
	Skin	23	9	E. 11 days fever	29.5.18	22. Excreta from offspring of T.F. lice, negative.	Lice fed on healthy men after first 24 hours.

AND INFECTIVITY OF EXCRETA (SECOND SERIES)

	Skin	1			12.5.18		Lice proved infective, Exp. 27 and 30.
	Skin	5	16	E. Shin pain. Sore mouth	10.6.18		
	Skin	6			17.5.18		
	Skin	6			1.6.18		
	Skin	7	13	C. Four febrile relapses	10.6.18	5. Laked blood, negative. 24. Excreta of lice fed on T.F. patient three days previously, negative.	
	Skin	7	13	E. 6 days fever	10.6.18		
	Skin	8			18.5.18	26. Excreta of lice fed on T.F. patient eight days previously, negative.	

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4.—INOCULATIONS WITH EXCRETA OF

(*C*).—Showing Interval between Infecting Feed and

Experiment Number.	Name.	T.F. Number.	Age.	Date of Coming Under Observation.	Date of Experiment.	Nature of Experiment.	Result.	Source of Infection.		Interval between Collection and Experiment.	Treatment of Inoculum.
								Name and Number.	Day of Disease.		
91	King, A.	596	62	16.5.18	19.6.18	Excreta of T.F. lice	–	Jones (380)	2 and 3	57 days	
45	O'Connor, J.	481	67	23.4.18	26.4.18	Excreta of T.F. lice	+	Jones (380)	2 and 3		
46	Saywell, G.	482	67	23.4.18	26.4.18	Excreta of T.F. lice	+	Jones (380)	2 and 3		
59	Howlett, R.	379	67	6.3.18	2.5.18	Excreta of T.F. lice	+	Jones (380)	2 and 3		

5.—INOCULATION WITH BODIES OF

9	Seymour, J.	300	69	2.2.18	5.2.18	Bodies of T.F. lice	+	Bligh (269)	11 to 23		Squashed

6.—TRANSMISSION

13	Evans, G.	362	65	20.2.18	26.2.18 19.3.18	Excreta of T.F. lice by mouth and inhalation	–	Various		24 hours	
14	Morris, T.	363	68	20.2.18	26.2.18 19.3.18	Excreta of T.F. lice by mouth and inhalation	–	Various		24 hours	
120	Backerman, G.	856	71	28.8.18	3.9.18	Excreta of T.F. lice by mouth	–	Hanlon (640)	2 to 25	15–21 days	

7.—INFECTION THROUGH

77	Cleary, T.	451	75	9.4.18	11.6.18	Excreta of T.F. lice	+	Steer (484)	27 and 28	24 days	
119	Pickett, W.	855	73	28.8.18	3.9.18	Excreta of T.F. lice	+	Hanlon (640)	2 to 25	15 days	

8.—VIABILITY

21	Doolan, G.	438	64	12.3.18	16.3.18	Old excreta of T.F. lice	+	Various		16 days	Exposure to sunlight
57	Beever, R. J.	567	78	3.5.18	7.5.18	Excreta of T.F. lice	+	Various		60 days	Kept at room temperature
95	Heyne, S. A.	621	30	1.6.18	7.7.18	Excreta of T.F. lice	+	Various		120 days	Kept at room temperature

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TRENCH FEVER INFECTED LICE—*continued*

INFECTIVITY OF EXCRETA (SECOND SERIES)—*continued*

Dosage. No. of Lice. C.C. of Blood. C.C. of Urine.	Site of Inoculation.	Interval in Days between Infection of Lice and Passage of Excreta.	Incubation Period.	Type of Attack.	Date of Discharge.	Summary of Previous Experiments.	Remarks.
900 lice	Skin	8			1.7.18	69. Scarification with T.F. urine, neg.	This sample failed to infect, Exp. 43.
	Skin	9	9	E. 'Saddle-back' fever	29.5.18		
	Skin	10	7	E. 'Saddle-back' fever	29.5.18		
	Skin	11	8	E. Very sudden onset. Fever 18 days	10.6.18	17. Excreta of normal lice, neg. 84. T.F. louse excreta heated 80° C. moist, neg.	Temp. 104·4° on first evening of disease.

TRENCH FEVER INFECTED LICE

11 lice	Skin		10	B. Very mild	13.3.18		

BY MOUTH TESTS

15 feeds		Unknown			15.4.18		Excreta from all boxes of lice infected to date.
9 feeds		Unknown			29.4.18		Excreta from all boxes of lice infected to date.
6 feeds		11 to 23			5.10.18		

CONJUNCTIVA

500 lice	Conjunctiva.	11 to 13	11	B. One relapse 8th and 9th days	17.7.18	41. Excreta T.F. lice 6th day from infecting feed, neg. 61. Excreta lice fed monkey inoculated T.F. louse excreta, neg.	
400 lice	Conjunctiva.	11 to 23	13	B.	5.10.18		

TESTS

	Skin		8	E. 10 days fever. Diarrhœa. 2 febrile relapses	13.5.18		Stools neg. Dys. (Dobell). Developed D.A.H.
	Skin		7	E. 9 days irregular fever. Max. 100·4°	29.5.18		Never sufficiently ill to stay in bed.
	Skin		13	E. 12 days irregular fever	27.9.18	Exp. 74. Excreta treated lysol	

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9.—DISINFECTION

Experiment Number.	Name.	T.F. Number.	Age.	Date of Coming Under Observation.	Date of Experiment.	Nature of Experiment.	Result.	Source of Infection.		Interval between Collection and Experiment.	Treatment of Inoculum.
								Name and Number.	Day of Disease.		
33	Jones, G.	380	68	6.3.18	6.4.18	Excreta of T.F. lice	+	Various		3 hours	Heated dry 56° C. for 20 mins.
58	Evans, G.	362	65	21.2.18	10.5.18	Excreta of T.F. lice	+	Jones (380)	2 & 3		Heated dry 65° C. for 20 mins.
73	Murray, S.	618	30	28.5.18	2.6.18	Excreta of T.F. lice	+	Steer (484)	27 & 28	12 days	Heated dry 68·2° C.–70° C. 20 mins.
84	Syred, F.	642	62	12.6.18	15.6.18	Excreta of T.F. lice	+	Steer (484)	27 & 28	30 hours	Heated dry 80·5° C. for 20 mins.
94	Chilvers, R.	722	62	26.6.18	2.7.18	Excreta of T.F. lice	-				Heated dry 100° C. for 20 mins.
34	Howlett, R.	379	67	6.3.18	6.4.18	Excreta of T.F. lice	-	Various		3 hours	Heated moist 80·5° C. for 10 mins.
82	Mitchell, E.	641	70	12.6.18	15.6.18	Excreta of T.F. lice	-	Steer (484)	27 & 28	6 hours	Heated moist 70° C. for 20 mins.
83	Hanlon, J.	640	76	12.6.18	15.6.18	Excreta of T.F. lice	-	Steer (484)	27 & 28	6 hours	Heated moist 60° C. for 20 mins.
62	Stephens, C.	420	66	20.3.18	18.5.18	Excreta of T.F. lice	+	Various			Ultra-violet rays, Barnard (Tube 3)
63	Stanton, M.	422	67	20.3.18	18.5.18	Excreta of T.F. lice	-	Jones (380)	2 & 3	19 days	Ground and soaked in distilled water 24 hours
74	Heyne, S. A.	621	30	1.6.18	5.6.18	Excreta of T.F. lice	-	Steer (484)	27 & 28	3 days	Soaked 2% lysol at 20° C. for 20 min.
75	Raine, A. O.	623	64	3.6.18	8.6.18	Excreta of T.F. lice	+	Steer (484)	27 & 28	3 days	Soaked 2% army soap in tap water 47° C. to 38° C. for 20 min.
80	Hicks, S.	627	28	8.6.18	14.6.18	Excreta of T.F. lice	-	Steer (484)	27 & 28	5 days	2% cresol, 18·5° C. for 22 mins.

10.—TESTS FOR PERCENTAGE

60	Barnaby, C.	452	66	9.4.18	12.5.18	Excreta of T.F. lice (10)	+	Woodhams (391)			
66	Andrews, F.	597	66	14.5.18	21.5.18	Percentage T.F. lice infected	+	Woodhams (391)			
71	Ball, H. F.	616	26	25.5.18	31.5.18	Percentage T.F. lice infected	+	Woodhams (391)			
79	Jones, S.	624	54	4.6.18	12.6.18	Percentage T.F. lice infected	+	Woodhams (391)		18 days	

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TESTS

Dosage. No. of Lice. C.C. of Blood. C.C. of Urine.	Site of Inoculation.	Interval in Days between Infection of Lice and Passage of Excreta.	Incubation Period.	Type of Attack.	Date of Discharge.	Summary of Previous Experiments.	Remarks.
	Skin		8	D. Febrile to 19th day	13.5.18	18. Excreta of normal lice, neg.	Inoculation repeated April 7th and 8th.
	Skin	9 to 11	12	E. Typical	10.6.18	13. T.F. louse excreta by mouth, neg. 38. T.F. blood on scarified skin, neg.	
500 lice	Skin	11 to 14	9	C. Three relapses	17.7.18		
500 lice	Skin	14 to 36	8	B. One relapse followed by influenza	9.8.18		
	Skin				28.7.18		? naturally immune.
	Skin				2.5.18	17. Excreta of normal lice, neg.	
500 lice	Skin	14 to 36			18.7.18		1 sample divided and used for Exp. 82, 83, 84.
500 lice	Skin	14 to 36			18.7.18		
	Skin		9	A. Very mild. 3 days. Max. 100·4°	10.6.18	25. Excreta from lice fed on T.F. patient 5 days previously, neg. 44. Dried T.F. blood by scarification, neg.	Excreta culturally sterile.
	Skin	9 to 14			10.6.18	26. Excreta of lice fed on T.F. patient 8 days previously, neg. 43. Excreta of lice fed on T.F. patient 8 days previously, neg.	? naturally immune.
500 lice	Skin	11 to 24			7.7.18		Control of nits, none hatched.
500 lice	Skin	11 to 24	10	D. Prolonged, with shin pain	27.6.18		Control of nits hatched 7.6.18.
500 lice	Skin	11 to 24			19.7.18		26.6.18. Influenza. Control of nits, none hatched.

OF LICE INFECTED

10 lice	Skin	16 to 18	9	B. Typical	10.6.18	39. Excreta of lice fed on T.F. patient 24 hours previously, neg.	
5 lice	Skin	19 to 25	7	E. Prolonged febrile	27.6.18		
1 louse (G) ♀	Skin	26 to 31	8	C. Very severe. Slight relapse 6th day	25.6.18		Same lice used in Exp. 60. 66, 71 and 79.
1 louse (H) ♀	Skin	27 to 32	9	B. Relapse 8th day	17.7.18		

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11.—HEREDITARY TRANSMISSION

Experiment Number.	Name.	T.F. Number.	Age.	Date of Coming Under Observation.	Date of Experiment.	Nature of Experiment.	Result.	Source of Infection. Name and Number.	Source of Infection. Day of Disease.	Interval between Collection and Experiment.	Treatment of Inoculum.
22	Woodhams, G.	391	63	14.3.18	18.3.18	Excreta of offspring T.F. lice	–	Various			
121	Traquair, R.	854	67	28.8.18	4.9.18	Excreta of offspring T.F. lice	+	Steer (484)	27 and 28	45 days	Eggs washed 1 % lysol 3 minutes and hatched in clean box
129	Parker, A. F.	881	58	14.9.18	20.9.18	Excreta of offspring T.F. lice	–	Steer (484)	27 and 28	61 days	As for Exp. 121 without lysol washing

12.—INFECTIVITY

69	King, A.	596	62	16.5.18	25.5.18	T.F. urine. One inoculation	–	Beswick (592)	19 to 25	36 hours	Centrifuged and deposit dried 37° C.
78	Devine, H.	625	26	5.6.18	11.6.18	T.F. urine daily for 10 days	–	Robinson (238)	1 to 10	3 days	Centrifuged and deposit dried 37° C.

13.—SUSCEPTIBILITY OF

61	Cleary, T.	451	75	9.4.18	17.5.18	Excreta of lice	–	Monkey 4. Arkwright	39		

14.—IMMUNITY

20	Dawson, H.	184	26	30.11.17	5.3.18	Immunity test. Ex. of lice	+	Various		30 hours	
28	Tullett, R.	320	60	8.2.18	28.3.18	Immunity test. Ex. of lice	–	Various			
29	Glover, R.	321	28	8.2.18	30.3.18	Immunity test. Ex. of lice	–	Reynolds (345) Exp. 10			
51	Wilson, R.	288	21	23.1.18	7.5.18	Immunity test. Excreta T.F. lice	+	Various		48 hours	
52	Lancaster, J. E.	313	22	8.2.18	7.5.18	Immunity test. Excreta T.F. lice	+	Jones (380)	2 and 3	9 days	
70	Robinson, E.	238	70	5.1.18	31.5.18	Immunity test. Excreta T.F. lice	+	Steer (484)	27 and 28	31 days	
76	Carter, W. R.	311	19	29.1.18	9.6.18	Immunity test. Excreta T.F. lice	–	Carroll (588)		6 days	
85	Beswick, A.	592	31	13.5.18	16.6.18	Immunity test. Excreta T.F. lice	–	Beswick (592)	16 to 19	13 days	

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OF INFECTION IN THE LOUSE

Dosage. No. of Lice. C.C. of Blood. C.C. of Urine.	Site of Inoculation.	Interval in Days between Infection of Lice and Passage of Excreta.	Incubation Period.	Type of Attack.	Date of Discharge.	Summary of Previous Experiments.	Remarks.
	Skin				13.4.18		
	Skin				5.10.18		Eggs laid up to 39 days from infection of lice. Infectivity of parents proved Exp. 64 and 75.
	Skin				15.10.18		See Exp. 121. Eggs from same box.

OF URINE

30 c.c. M. and E. daily	Skin				19.6.18		Beswick typical 5 day fever (France).
30 c.c. M. and E. daily	Skin				18.7.18		

MONKEYS TO TRENCH FEVER

	Skin	24			11.6.18	41. Excreta of lice fed on T.F. patient 6 days previously, neg.	Monkey inoculated T.F. louse excreta.

TESTS

	Skin		9	C. Two febrile relapses. Shin pain	27.4.18		Original infection in France. Re-infection on 102nd day. No symptoms.
	Skin	Up to 35 days			23.4.18	11. T.F. louse excreta, pos.	Immune 30th day. Vague pains.
	Skin	Up to 32 days			23.4.18	12. T.F. louse excreta, pos.	Immune 31st day. Spleen palpable.
	Skin	12	8	C. 'Spikes' of fever	7.6.18		Not immune 115th day. D.A.H.
	Skin	13	13	A. Very mild without relapse	21.6.18		Not immune 117th day. Dyspnœa and pains.
	Skin	21 to 23	8	B. Relapse 6th, 7th, 8th days	13.7.18	3. 5 c.c. whole blood. Result, positive	Not immune 139th day. Original infection, Exp. 3.
	Skin	12 to 20			18.7.18	(35) Immune to whole blood i.v., 62nd, 98th days (49)	Immune 134th day. Infectivity of excreta doubtful.
400 lice	Skin	11 to 19			18.7.18		Immune to excreta own lice 48th day.

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14.—IMMUNITY

Experiment Number.	Name.	T.F. Number.	Age.	Date of Coming Under Observation.	Date of Experiment.	Nature of Experiment.	Result.	Source of Infection.		Interval between Collection and Experiment.	Treatment of Inoculum.
								Name and Number.	Day of Disease.		
86	Lloyd, O.	578	27	6.5.18	18.6.18	Immunity test. Excreta T.F. lice	+	Nurse Pullan(620)	6 to 8	A few hours	
90	Tyler, H.	374	30	6.3.18	19.6.18	Immunity test. Excreta T.F. lice	-	Tyler (374)	116 to 118	16 days	
98	Reynolds, G.	345	68	13.2.18	23.7.18	Immunity test. Excreta T.F. lice	-	Various		154 days	Balance of excreta which infected him in Exp. 10
99	Jordan, C.	299	66	2.2.18	23.7.18	Immunity test. Excreta T.F. lice	+	Beswick (592)	16 to 19	50 days	
104	Carter, W. R.	311	19	6.2.18	10.8.18	Immunity test. T.F. louse excreta	+	Beswick (592)	16 to 19	68 days	8 mgm. in 0·5 c.c. N.S.
105	Reynolds, G.	345	68	13.2.18	20.8.18	Immunity test. T.F. louse excreta	-	Beswick (592)	16 to 19	78 days	
114	Libby, J.	638	43	10.6.18	2.9.18	Immunity test. T.F. louse excreta	-	Steer (484)	27 and 28	110 days	Emulsified 1 c.c. N.S.
35	Carter, W. R.	311	19	29.1.18	29.3.18	Immunity test	-	Brett (341)	63	1 minute	Citrated, whole blood
37	Mead, S. V.	292	21	17.1.18	15.4.18	Immunity test. Whole blood i.v.	-	Jones (380)	2	1 minute	Citrated
49	Carter, W. R.	311	19	29.1.18	4.5.18	Immunity test. Whole blood i.v.	-	Saywell (482)	2	1 minute	Citrated.
65	Tyler, H.	374	30	6.3.18	20.5.18	Immunity test. Whole blood i.v.	-	Goodman (569)	7	1 minute	Citrated
89	Reynolds, G.	345	68	14.2.18	18.6.18	Immunity test. Whole blood	-	Raine (623)	1	5 mins.	Citrated
103	Libby J.	638	43	10.6.18	5.8.18	Immunity test. Whole blood	-	Mitchell (641)	7	1 minute	Citrated, equal parts
108	Bass, A.	662	19	16.6.18	23.8.18	Immunity test. Whole blood	-	Carter(311)	4	1 minute	Citrated, equal parts
110	Du Faur, W.	675	32	19.6.18	27.8.18	Immunity test. Whole blood	-	Carter(311)	8	3 mins.	Citrated, equal quantities
111	Pecksen, T. H.	737	22	2.7.18	27.8.18	Immunity test. Whole blood	+	Carter(311)	8	3 mins.	Citrated, equal quantities
112	Kirkland, E. O.	801	26	7.7.18	27.8.18	Immunity test. Whole blood	+	Carter(311)	8	3 mins.	Citrated, equal quantities
115	Carpenter, W. H.	268	43	16.1.18	3.9.18	Immunity test. Whole blood	-	Pecksen (737)	2	8 mins.	Citrated, 15 c.c. sodium citrate sol.
116	Evans, G.	362	65	20.2.18	3.9.18	Immunity test. Whole blood	-	Pecksen (737)	2	7 mins.	Citrated, 15 c.c. sodium citrate sol.
125	O'Connor, J.	481	67	23.4.18	12.9.18	Immunity test. Whole blood	-	Finnis(852)	1	12 mins.	Citrated, 15 c.c. 1·8 % sod. cit. sol.

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TESTS—*continued*

Dosage. No. of Lice. C.C. of Blood. C.C. of Urine.	Site of Inoculation.	Interval in Days between Infection of Lice and Passage of Excreta.	Incubation Period.	Type of Attack.	Date of Discharge.	Summary of Previous Experiments.	Remarks.
100 lice	Skin	12 to 20	10	D. Febrile relapse 7th day	19.7.18		Pullan, accidental infection in hosp. Lloyd not immune on 52nd day of disease.
	Skin	14 to 17			18.7.18	Immune to T.F. blood, 119th day, Exp. 65	On 149th day was immune to lice fed on himself.
	Skin				19.8.18	10. Excreta of T.F. lice, pos. 89. 20 c.c. whole blood T.F. i.v., negative	Immune on 154th day from original infection.
400 lice	Skin	11 to 19	9	F. Periodic intermittent fever	19.8.18	7 and 19. Both 5 c.c. whole blood T.F. i.m.	Not immune on 132nd day of disease.
8 mgm.	Subcut.	11 to 19	10	F. Periodic intermittent fever	2.9.18	Immunity tests 35 and 49. Whole blood	Infectivity of excreta proved by Exp. 99.
						76. Louse excreta. All negative	Not immune on 198th day of disease.
20 mgm.	Skin	11 to 19			18.9.18	10. T.F. louse excreta, pos. 89. Whole blood, negative 98. T.F. louse excreta, neg.	Immune on 182nd day of disease.
4 mgm.	Subcut.	11 to 37			28.9.18	87. 0·5 c.c. whole blood i.v. Result, positive	Infectivity of excreta proved by Exp. 64.
						103. 20 c.c. whole blood i.v. Result, negative	Immune on 76th day of disease.
5 c.c.	Vein				4.5.18		Immune 62nd day of relapse. Pains in head and legs.
5 c.c.	Vein				31.5.18		Immune 99th day. D.A.H., etc.
5 c.c.	Vein				8.6.18	35. Immunity test. Whole blood, negative	Immune 98th day of relapse. Pain in legs.
4 c.c.	Vein				17.6.18		Immune 119th day. No symptoms.
20 c.c.	Vein				18.7.18	10. Excreta T.F. lice. Result, positive	119 days since original infection, Exp. 10.
20 c.c.	Vein				2.9.18	87. 0·5 c.c. whole blood i.v., positive	Immune on 48th day of disease.
20 c.c.	Vein				13.9.18		Immune on 80th day of disease.
20 c.c.	Vein				21.9.18		Immune on 85th day of disease.
20 c.c.	Vein		6	C.	27.9.18		Not immune on 70th day of disease.
20 c.c.	Vein		8	D.	27.9.18		Not immune on 65th day of disease.
50 c.c.	Vein				28.9.18	42. Excreta T.F. lice by scarification, positive	Immune on 122nd day of disease.
50 c.c.	Vein				28.9.18	58. T.F. louse excreta heated dry 65° C., 20 minutes, positive	Immune on 116th day of disease.
50 c.c.	Vein				5.10.18	45. Louse excreta, positive	Immune on 139th day of disease.

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15.—RICKETTSIA

Experiment Number.	Name.	T.F. Number.	Age.	Date of Coming Under Observation.	Date of Experiment.	Nature of Experiment.	Result.	Source of Infection.		Interval between Collection and Experiment.	Treatment of Inoculum.
								Name and Number.	Day of Disease.		
100	Donnelly, T.	643	70	12.6.18	24.7.18	Gut contents T.F. louse. Rickettsia, negative	–	Arkwright	32	2 hours	Louse soaked lysol 2½ % and washed Stomach removed and emulsified N.S.
101	Morris, S.	668	84	17.6.18	24.7.18	Gut contents T.F. louse. Rickettsia, positive	+	Arkwright	32	2 hours	Louse soaked lysol 2½ % and washed Stomach removed and emulsified N.S.
142	Backerman, G.	856	71	28.8.18	5.10.18	Inoculation with louse. Rickettsia, negative	–	Finnis(852)	5	5½ hours	Emulsion in 2 drops N.S.
143	Traquair, R.	854	67	28.8.18	5.10.18	Inoculation with louse. Rickettsia, positive	+	Finnis(852)	5	5½ hours	Emulsion in 2 drops N.S.

16.—TRANSMISSION

113	Langley, W.	626	28	6.6.18	27.8.18	Transmission by bugs	–	Mitchell (641)	1	Half a day	Guts emulsified in N.S. and added to emulsion of their excreta

17.—EFFECT OF TEMPERATURE ON

117	Thomson, J. W.	851	72	27.8.18	3.9.18	Effect of temp. on development of T.F. virus in louse	+	Arkwright			Lice kept 27° C.
118	Finnis, J.	852	57	27.8.18	3.9.18	Effect of temp. on development of T.F. virus in louse	+	Arkwright			Lice kept 17° C.

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EXPERIMENTS

Dosage. No. of Lice. C.C. of Blood. C.C. of Urine.	Site of Inoculation.	Interval in Days between Infection of Lice and Passage of Excreta.	Incubation Period.	Type of Attack.	Date of Discharge.	Summary of Previous Experiments.	Remarks.
1 louse	Skin	11			19.8.18	88. Whole blood T.F. ½ c.c. scarified into skin	
1 louse	Skin	11	9	E. Severe, short	26.8.18	92. Excreta of lice fed on old T.F. case	
1 louse	Skin				4.11.18	120. Louse excreta by mouth, negative	
1 louse	Skin		9	B.	1.11.18	121. Excreta from offspring T.F. lice, negative	

BY BUGS

3 bugs	Sub-cut.	28			25.9.18		1.12.18. still fit.

DEVELOPMENT OF T.F. VIRUS IN LOUSE

1 mgm.	Skin		10	B.	19.10.18		Rickettsia present in excreta.
1 mgm.	Skin		9	B.	9.10.18		No Rickettsia detected in excreta.

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APPENDIX II

TABLE X.—*Affording evidence that Trench Fever infection caused by the biting of infected lice is due to accidental contamination of the bites by the excreta and is not the natural means of conveyance.*

The table summarises the attempts to infect four men with the bites of trench fever infected lice, the experiments controlling one another by the interchange of the boxes of lice.

The first column gives the number of the box; the second, the source of the infection of the lice (for fuller information of these see text); the third, the dates of the infecting feeding; the fourth, the period of the disease during which the lice were infected; the fifth, the number of infected lice contained in the box when it was first fed on the healthy man. Under the various dates the remaining columns show a number indicating how many days previously the lice had received their first infecting feed, and the initial of the man on whom they were fed in the morning (above), and the evening (below). In these columns are also given the results of the inoculations of the excreta, when these were carried out, proving the infectivity or otherwise (+ or —) of the excreta on those days.

Our evidence shows that the excreta of trench fever infected lice becomes infective before the twelfth day after their first infecting feed, and sometimes as early as the fifth (Experiment 53); that the excreta remains infective until the death of the louse (Experiment 79); that most of, and possibly all, the lice become infective (pp. 39 and 40). The vast majority of the bites recorded in the table were therefore from lice the excreta of which were infective.

Of the four men used in this series one only, Jackson (Experiment 48), developed trench fever, doing so on April 29, fourteen days after the lice began to feed upon him. Consideration of the table will show that, with two exceptions, all the boxes of lice which were fed on him also fed on one or more of the other

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23	24	25	26
32 P J	33 J J	34 J J	35
36 J P	37 P P	38 P P	39
34 B B	35 B B	36 B	
34 J P	35 P P	36 P P	37
29 J J	30 J J	31 J J	32
22 J P	23 P P	24 P P	25
13 B B	14 B B	15 B B	16
22 P J	23 J J	24 J J	25
...	...	...	...
...	...	...	...
...	...	...	...
8 B B	9 B B	10 B B	11
. – Exp. 43 . – ?Exp. 91	Exc. + Exp. 45	Exc. + Exp. 46	Exc. + Ex
...	...	...	...
...	...	...	...

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men after the day on which the infectivity of the excreta was either proven or might be assumed. The two exceptions, Boxes 146 and 153, fed upon him only on the day when he developed fever and on the two days previous to this, so that it is certain he did not acquire his fever from these, as the incubation period would be too short.

Since, therefore, all four men were exposed so similarly to the same very numerous chances of infection, and only one of them became infected, it may be fairly assumed that it was by the accidental contamination of the bites by the infective excreta that he became infected, and that infection by this means does not readily take place.

The summary of the four experiments is given below. In Experiment 47 no chiffon intervened between the lice and the skin, while in Experiments 40, 48, and 50 the lice fed through chiffon. For further details of these experiments the text (pp. 55 and 56) should be consulted.

Experiment Number.	Name.	Number of Days over which Feeding extended.	Number of Bites.	Result.	Incubation Period.	Period of Observation after Louse Feeding began.
40	Riches	22	4,945	–	...	45
47	Prince	15	23,821	–	...	22
48	Jackson	15	25,609	+	14 days	...
50	Bell	15	21,908	–	...	61

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APPENDIX III

LETTER from Patient, invalided from the Army, whose case is described in full under 'Chronic Disease.' Letter dated 29.4.18, or 25 months from onset of trench fever.

MAJOR BYAM.

DEAR SIR,—I thought you would like me to write. I have felt, since I left hospital, better in myself.

I have had three distinct returns of the fever, which necessitated my staying in the house, the symptoms on these occasions being loss of energy, headache, some dizziness, and my legs ache on awakening.

I have days when I feel very well, and on these days I try and do some light work around the house.

I find I am very weak, and when working I have to stop, because I have felt too weak to do any more. I just go and lie down.

I feel fairly well as long as I remain quiet, but on exertion I have to lie down and rest.

I have not started work yet, because I am not strong enough to do a day's work.

I have not had any lice on me since I left hospital.

I am better since I left. I feel better at longer times together, but am very weak. I am going down to Bournemouth for a few weeks to try and regain my strength.

When once one becomes a victim of trench fever it takes a lot of moving.—I remain, yours obediently,

T. H. G.

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APPENDIX IV

By Lieut. R. H. VERCOE, R.A.M.C.

A SUMMARY of the Report of the Commission of the American Red Cross Research Committee on Trench Fever.

Members of the Commission—Maj. Richard P. Strong, M.R.C.; Maj. Homer F. Swift, M.R.C.; Maj. Eugene L. Opie, M.R.C.; Capt. Ward J. MacNeal, M.R.C.; Capt. Walter Baetjer, M.R.C.; Capt. A. M. Pappenheimer, M.R.C.; Capt. A. D. Peacock, R.A.M.C.(T.); (subsequently attached) 1st Lieutenant David Rapport, M.C., A.E.F.

The work of the Commission was begun at the end of January 1918, and was carried on during the following two months at a B.E.F. Stationary Hospital, which was near enough to the line to secure cases of trench fever in the very early stages of the disease.

Volunteers for the transmission of the disease were obtained from the American Army, and were subjected to elaborate preliminary examination, clinical and bacteriological, before being used, in order to exclude the unfit. Eighty-two volunteers were used, the disease was produced in 62 of them, and 103 human experiments were performed. The work was undertaken because the loss of man-power by trench fever in the British Army exceeded from one to two-thirds of all sickness. This threat to the American Army required immediate attention.

CONCLUSIONS OF THE COMMISSION

(1) That trench fever is a specific infectious disease; that it is not a modified form of typhoid or paratyphoid fever, nor related to them.

(2) That the causative organism is a resistent filterable virus.

(3) That the virus causing trench fever is present particularly in the plasma of the blood of trench fever cases, and that such plasma will produce the disease on inoculation into healthy individuals.

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(4) That the disease is transmitted by the louse *P. humanus* (Linn.), var. *corporis*, and that this is the important and common means of transmission ; that the louse may transmit the disease by its bite alone, the usual manner of infection, or the disease may be produced artificially by scarifying the skin and rubbing in a small amount of the infected louse excrement.

(5) That a man may be entirely free from lice at the time he develops trench fever, the louse that infected him having left him some time previously as its host, and that the louse need only remain upon the individual for a short period of time in order to infect him.

(6) That the virus of trench fever is also sometimes present in the urine of trench fever cases, and occasionally in the sputum, and that the disease may be produced in man by the introduction of the virus in the urine or sputum through the scarified or otherwise abraded skin.

Recommendations

(*a*) That greater efforts must be made to keep soldiers free from infestation with lice, in order to save man-power for the armies.

(*b*) That all patients, particularly on entering hospital, should undergo immediate and complete disinfestation.

(*c*) That patients entering hospital should be carefully bathed and subsequently sponged with alcohol.

(*d*) That their clothing and blankets should be removed, whether obviously infested or not, and sterilised at a temperature of at least 70° C. moist heat for half an hour.

(*e*) That trench fever patients should be treated in separate wards and inspected daily for lice.

The following is a *résumé* of the evidence on which these conclusions are based :

(1) (*a*) That the *louse* is capable of transmitting trench fever. Twenty men exposed to continuous contact with infective lice kept on the bare arm in cells strapped thereon, and living under approximately natural conditions ; cells removed for short intervals to permit patients in some cases to scratch or scarify the skin or crush the lice. The louse excrement was not removed, but left on the skin. Results—14 were positive, 6 negative. Of the negatives some scratched or were scarified, *e.g.* Driscoll (page 194) and Quinn (page 200), 7 artificial scarifications on

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6 different occasions. Of the positives some were not scratched nor scarified, *e.g.* Worley (page 185), who, however, had an excoriation from friction of the cell tapes. Incubation periods were 15–35 days.

(*b*) That trench fever is not spread by intimate contact alone if the contacts are kept entirely free of lice and infective louse excreta. Eight healthy volunteers remained healthy though living and sleeping with experimental cases suffering from acute trench fever.

(2) That transmission is *not hereditary* in the louse, *i.e.* the ova of infective lice are not themselves infective when matured. Two men exposed to newly hatched lice from ova of infective parents under same conditions as above. Results both negative.

(3) That *normal* lice do *not* cause trench fever. Four men, three later proved to be non-immune, exposed (under same conditions as above) to normal uninfected lice. Results all negative.

(4) That the louse can transmit trench fever by the *bite alone.*

(*a*) Three men exposed to contact with lice kept on the arm in closed boxes, biting the flesh through interposing chiffon. No scratching, scarification, nor crushing. Results all positive. Detailed extracts :

Emhoff (page 249), continuous exposure for 3½ days to 170–80 lice. (Page 250) 'On the upper arm, owing to the adhesive, the skin had been broken but is scabbed; no contaminated material from the cell allowed near it.' One special area sore and swollen. No gross lesions present. 'The skin was only slightly soiled by louse excrement, though many dead and crushed insects were in contact with it.' Incubation period 15 days.—Humphreys (page 251), continuous infestation for 4½ days with 80–66 lice. Incubation period 14 days. 'The subject rubbed the dressings, but not roughly.' 'Excrement was present in abundance on the bitten area and 6 dead and crushed lice were picked off the soiled skin.' Burke (page 252), continuous exposure for 4½ (intermittent for 3 days later) to 66–38 lice. 'The skin was soiled by a considerable amount of louse excrement, while 3 dead and crushed lice were found among it.' Incubation period 30 days.

(*b*) Transmission by bite alone continued; special attempt to exclude other factors than bite. Two men exposed for half-hour periods twice daily for 21 days to lice biting through clean chiffon. Results both positive. 'The arm was held with the

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box underneath, so that the lice were compelled to bite upwards through the chiffon.' The feeding lasted half an hour when the box containing the lice was removed and placed in the incubator. 'At each feeding time a clean chiffon cover was stretched over the mouth of the box.' 'One source of contamination of the circum-oral mouth parts always existed in the fæces of the louse-box.' The bitten areas were cleansed from infective matter after feeding; for the first 5 days by a swab dipped in 2 per cent. lysol, or methylated spirits or simple soap and water; for the ensuing 16 days the dry fæcal granules were removed carefully one by one with a camel hair brush moistened in methylated spirit. The skin was stretched and a reading glass used to detect the small specks of excrement. After this the area was placed beneath a rapid stream of running water. 'There was general reddening of the arm due to the increasing number of bitten areas.' 'The irritation from the exposure was largely the result of the bites as the men did not aggravate the bitten area by scratching, the utmost they permitted themselves being to rub it with the flat of the hand.' The bitten areas of Perry became deeply swollen as a result of œdema, while Falls showed a number of superficial papules. Perry contracted the disease in 27 days (average louse contact 500), Falls in 38 days (average 250 lice) from first day of contact with lice known to be already infective.

The Commission concludes:—(1) 'That lice may transmit the disease to a subject under conditions in which the injection of saliva appears to be a more prominent feature than the unavoidable presence of minute amounts of louse excrement upon the bitten areas during the feeding process.' (2) That the incubation period appears longer than by continuous cell method.

(5) That transmission is *not necessarily mechanical.*

Infective lice were fed for 48–60 hours on 5 healthy men, and then transferred to 5 other healthy men. The 5 latter all contracted trench fever.

Of the 5 intermediate healthy men, 4 also contracted the disease, thus showing that *multiple infection* may be caused by the same group of lice.

(6) Further summaries (page 271). In 20 positive biting experiments the incubation period was never less than 14 days.

(7) Lice may remain infective for at least 10 days, and possibly 13.

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(8) There is evidence that if the virus undergoes development in the louse, it requires 6–10 days to do so; there is a little evidence that suggests the minimum incubation period to be about 4 days (page 277).

(9) Lice were certainly rendered infective in 9½ days and probably in 6–7 by feeding them on a trench fever patient from the latter part of the first to the seventh days of illness inclusive and then on a healthy man for about 3 days.

Artificial transmission shows:

(*A*) By inoculation into scarified skin.

(1) That the *Excreta of lice are infective.* Four experiments; infective louse excreta rubbed into scarified skin area. Results, all positive; incubation period 7–10 days, average 9 days. Four later similar experiments. Results all positive; incubation periods 9, 9, 11, 11 days respectively.

(2) That the *Saliva and Sputum* of the patient may be infective. Saliva and sputum of patient rubbed into scarified skin. Five experiments. Results, 1 positive, 4 negative.

(3) That the *Urine* may be infective. Urinary sediment rubbed into scarified skin. Eight experiments. Results, 5 positive, 3 negative; incubation period 6–30 days.[1]

(4) That the *Fæces are not infective.*

Fæces rubbed into scarified skin. Three experiments. Results, all negative.

(*B*) By inoculation intravenously.

(1) That the *Blood is infective.*

(*a*) whole blood,	results,	12 positive, 1 negative (92·3 per cent. +)
(*b*) citrated whole blood,	results,	3 positive, 0 negative (100 per cent. +)
(*c*) whole plasma,	results,	5 positive, 0 negative (100 per cent. +)
(*d*) washed blood cells,	results,	3 positive, 1 negative (75 per cent. +)
(*e*) filtered blood,	results,	All but one certainly negative.

Filtered blood (centrifuged filtered (*a*) plasma, (*b*) serum, (*c*) ground up corpuscles respectively).

[1] It is interesting to note that in examining the experimental records it is found that the urine passed on the tenth day or later was shown to be infective, whereas in the two cases where the urine was passed in the first few days only of the disease the results were negative, which bears an analogy with relapsing fever.

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The incubation period varied from 5–20 days. The blood appears to be most infectious on the 1st and 2nd days of the disease, ' and more infectious during the first attack than during the relapse.' From these blood inoculation experiments it is evident that the virus is present in the blood, and particularly in the plasma.

(2) That the *Virus is filterable.*

Attempts to filter the virus present in the blood gave negative results (as above), but this is explained very lucidly as being probably due to clogging of the filter pores by the albuminous constituents of the blood medium in which the virus was suspended, and considerable space is devoted to a very interesting discussion of the whole subject of filtration and resistance of ultramicroscopic viruses in general.

Therefore experiments were made with a saline suspension of the virus present in infective human urine and in infective louse excreta. Results, 3 positive, 2 negative.

(*a*) 46 c.c. normal saline suspension of urinary sediment (shown to be infective in controls by inoculation into scarified skin) was filtered under 760 mm. negative pressure for 2½ hours through unglazed porcelain Chamberlain L filter. *Bacillus typhosus* was chosen as a control to test the efficiency of the filter to hold back all but ultramicroscopic organisms; it was shown to hold back *B. typhosus* both previously and subsequently under the same conditions. Aerobic and anaerobic cultures of the filtrate remained sterile. The filtrate was inoculated intravenously into 2 men (15 c.c. each). Results, one positive (incubation 21 days), one negative.

(*b*) 60 c.c. normal saline suspension of louse excreta (shown to be infective by skin inoculation into controls) was filtered exactly as above, and the filtrate inoculated intravenously into 3 men. Results, one negative (10 c.c.), 2 positive (10 c.c. and 6 c.c.). Incubation period 5 days and 20 days.

The Resistance of the Virus

Louse excreta containing the virus from many sources was thoroughly *ground to a fine powder,* and divided into five portions, each of which was spread out in a Petri dish in a *thin uniform layer,* except one which was suspended in saline.

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The tests and results for each portion were as follows:

Time.	Conditions.	Temperature.	Result.
(1) 3 hours	suspension in 30 c.c. saline	at room temp.	virus resistent
(2) 3 hours	exposure to air	at room temp.	virus resistent
(3) ½ hour	in closed water bath	at 60°C. moist	virus resistent
(4) ½ hour	in closed water bath	at 70°C. moist	virus destroyed
(5) ½ hour	in closed water bath	at 80°C. moist	virus destroyed

Specific Nature of Trench Fever

That trench fever is not a modified form of typhoid or paratyphoid was demonstrated as under:

(1) No bacterial growth was obtained in 200 examinations of blood, stools, and urine, whereas in clinical cases of infection with the enteric group at least 20 per cent. such examinations were positive.

(2) No bacterial substances affecting the growth of the enterica organisms were ever obtained from the blood of trench fever patients.

(3) The agglutination titre determined by Dreyer's method never showed any constant or characteristic fluctuations in vaccinated men who developed trench fever.

Incubation Period

Varies with *method* of infection, and probably with *size of dose*.

(1) Intravenous blood, ... incubation 5-20 days.
(2) Intravenous filtrate of urine and louse excreta, ,, 5-22 ,,
(3) Artificial scarification with louse excreta, . ,, 7-11 ,,
(4) Artificial scarification with urinary sediment, ,, 6-30 ,,
(5) Onset of disease from date lice first placed on patient, ... ,, 14-38 ,,
(Lice known to be infective from the first day.)

In the blood inoculation experiments, 'in those cases with one exception in which the incubation period was long, the individuals were inoculated with blood either taken late in the disease or during the relapse of the fever. The development of immune bodies may be sufficient to prolong the incubation period.' Contrasting the above incubation periods in inoculation respectively by blood intravenously, by scarification, and by louse infestation, 'it seems clear that in nature the virus either (*a*)

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multiplies within the louse, or (*b*) undergoes a cycle within it before infecting man, or (*c*) that the amount of virus inoculated by the louse is so small that the incubation period is much lengthened' (page 58). In this connection it is interesting to compare the incubation periods of typhus and of European relapsing fever, which are also louse-borne diseases. In typhus fever, natural human incubation usually 9–20 days, but experimental monkeys may give as long as 26 or even 41 days (Nicolle), page 15. In relapsing fever, clinical experience gives 2 days or less to 12 days, while experimental inoculation gives 6–8 days.

Symptoms and Signs

Experimental Disease	Natural Disease
Prodromal — sometimes, with headache, malaise, and chilliness from a few hours to some days before onset.	*Prodromal*—occasionally, with slight headache, limb pain, and slight fever.
Onset — usually *sudden*, with chill mild to severe.	*Onset*—usually *sudden*, accompanied by—
Headache, almost always, usually frontal and behind eyes.	*Headache* and pain behind eyeballs.
Dizziness and *Malaise* varying from lassitude to extreme weakness within a few hours of onset.	*Dizziness*.
Conjunctival Congestion (95 per cent. cases) appearing early and with or before each relapse.	*Conjunctival Congestion*.
Nystagmus lateral (85 per cent. cases) especially on lateral extreme deviation of eyes.	*Nystagmus lateral*.
Pain in back (lumbar), calves and thighs; shin pain not till 3rd day (77 per cent. cases).	*Pain* in back and legs, including shin pain.
Temperature—not so characteristic as commonly supposed (see below).	*Temperature* — sharp rise to about 103° F., relapsing later in over 50 per cent. cases.

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Anorexia usually, with sometimes nausea and vomiting.

Spleen, enlarged in 85 per cent. cases.
Liver not palpable.
Spots appear in 50 per cent. in louse expts., in 83 per cent. in blood expts.; often seen a few hours after onset.

Frequency of micturition, once or twice only.
Leucocytosis usually, may be normal or leucopenia.
Tongue usually furred heavily, clean at edges; abdominal pain common but gastro-intestinal symptoms absent.
D.A.H.—absent.
The *Fever* chart of many patients will not conform with any of the definite classifications (cf. page 292). In the so-called typical form there was a sharp rise with sharp fall all within 24 hours and repeated every 5 or 6 days.
The intervals between the relapses may be more irregular, 4-day, or 9-day intervals, as though a relapse had been skipped, or longer. Instead of a sharp spike we may get 2-day cycle at each relapse. 'Again, the first bout of fever may extend over 3 or 4 days, to be followed by either a spike or another long course.' 'Finally, we have

Spleen, enlarged in 70–80 per cent. cases.
Liver not palpable.
Spots appear (70–80 per cent. cases) on 2nd or 3rd day or during relapse; multiple and erythematous, over chest, back, and abdomen.
Frequency of micturition common.
Leucocytosis usually, may be normal or leucopenia.
Urine often shows a trace of albumen, but no true nephritis.

D.A.H.—common.
The *Fever* may be (*a*) a short attack lasting for about a week, with sometimes but not always, after a few days, a single short rise.
(*b*) a more prolonged initial fever, sometimes lasting for 6 or 7 weeks, with relapses not distinctly marked.
(*c*) A more regularly relapsing fever with more or less definite normal intervals, lasting from 5 to 7 days.
(*d*) Many variations of these types are also seen, *e.g.* a long fever lasting from 40 to 60 days or more, with only slight remissions.
'The number of relapses varies greatly' (page 17).

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a large group of cases in which the course of the fever can be described only by its tendency to relapse.' 'The importance of carefully noting the symptoms as well as the temperature is brought out by the fact that not infrequently we observed a relapse of pain or tenderness, or an increase of the pulse rate, at the time of an anticipated relapse, while the temperature remained practically normal.'

Prognosis:

'Usually the patient recovers in from 5 to 6 weeks from the time of onset.' 'In other cases, however, the disease may be greatly prolonged' (page 17). Never fatal (page 308).

Diagnosis

'While no one of these symptoms given above can be regarded as characteristic or constant, the presence of several or all of them usually serves to make the diagnosis of trench fever accurate' (page 16). 'The diagnosis must in many instances be made by the exclusion of other infections, and where clinical or laboratory examinations have not been performed cases of trench fever might sometimes very easily be confused with influenza, modified typhoid, or paratyphoid fever, malaria, European relapsing fever, dengue, phlebotomus fever, or mild epidemic jaundice.'

In atypical cases 'careful daily examination for the positive physical signs of the disease—in the eye, spleen, skin, and areas of tenderness combined with complete temperature and pulse charts—and the absence of the positive features of other diseases, will often help in arriving at a correct diagnosis' (page 307).

Differential Diagnosis.—'From influenza by the scarcity of the respiratory symptoms and signs at onset, by the rash, by the peculiar hardness of the spleen, by the areas of pain and tenderness, and by the relapsing character of the fever symptoms.'

From typhoid and paratyphoid fever by more sudden onset and rapid development of symptoms, absence of intestinal symptoms, peculiar hardness of spleen, tender areas, leucocytosis usually, absence of T.A.B. bacilli in blood, stools, and urine (page 307).

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From malaria by different temperature course, less severe rigors, the rash, the tender areas, and by blood examination.

From spirochœtal relapsing fever—the onset, pain, distribution and rash are somewhat similar in both, but in relapsing fever there is liver enlargement, response to salvarsan, spirochœtes in blood, and 'the course of the fever is prolonged and high, and the fall by crisis on the 6th or 7th day, with a relapse on the 14th day' (page 308).

From dengue fever—onset and pain distribution similar in both. 'The course, however, is short in dengue, with an intermission or remission on the 3rd to 5th day.' 'There is a leucopenia in dengue, while in trench fever there is usually a leucocytosis.'

In typhus fever there is step-ladder temperature, severe increasing toxic symptoms, and a shorter course, which is often fatal.

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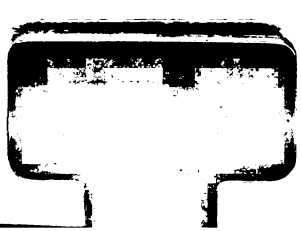

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